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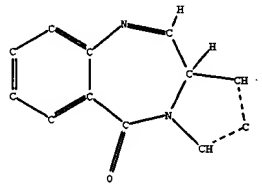
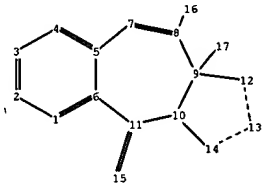
Sept. 28, 2001

C:\STNEXP4\QUERIES\09763767.str

L8





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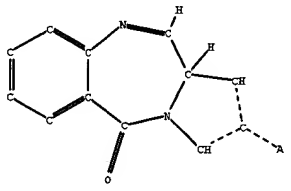
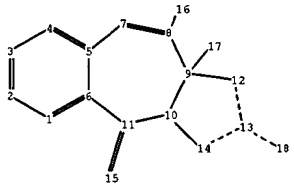
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14
chain bonds :
8-16 9-17 11-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-11 7-8 8-9 9-10 9-12 10-11
10-14 12-13 13-14
exact/norm bonds :
5-7 6-11 7-8 8-9 9-10 9-12 10-11 10-14 11-15 12-13 13-14
exact bonds :
8-16 9-17
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS

C:\STNEXP4\QUERIES\09763767a.str

214





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ring nodes :
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chain bonds :
8-16 9-17 11-15 13-18
ring bonds :
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10-14 12-13 13-14
exact/norm bonds :
5-7 6-11 7-8 8-9 9-10 9-12 10-11 10-14 11-15 12-13 13-14 13-18
exact bonds :
8-16 9-17
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
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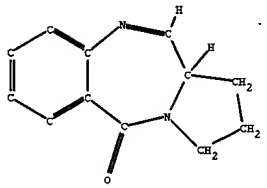
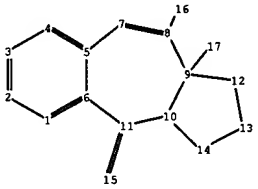
18:CLASS

C:\STNEXP4\QUERIES\09763767b.str

L13





chain nodes :
15 16 17
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14
chain bonds :
8-16 9-17 11-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-11 7-8 8-9 9-10 9-12 10-11
10-14 12-13 13-14
exact/norm bonds :
5-7 6-11 7-8 8-9 9-10 9-12 10-11 10-14 11-15 12-13 13-14
exact bonds :
8-16 9-17
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS

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=> D HIS

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     FILE 'REGISTRY' ENTERED AT 18:03:09 ON 28 SEP 2001

     FILE 'STNGUIDE' ENTERED AT 18:05:04 ON 28 SEP 2001

     FILE 'REGISTRY' ENTERED AT 18:05:47 ON 28 SEP 2001
L7              STRUCTURE UPLOADED
L8              QUE L7
L9           12 S L8
L10         250 S L8 SSS FUL

     FILE 'CAPLUS' ENTERED AT 18:08:53 ON 28 SEP 2001
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     FILE 'REGISTRY' ENTERED AT 18:10:18 ON 28 SEP 2001
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L14             STRUCTURE UPLOADED
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L16          10 S L13  SUB=L10 SAM
L17           2 S L14  SUB=L10 SAM
L18         172 S L13  SUB=L10 FUL
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     FILE 'CAPLUS' ENTERED AT 18:15:31 ON 28 SEP 2001
L20          86 S L18
L21          50 S L19
L22         122 S L20 OR L21
L23          88 S L22 AND JOURNAL/DT
L24           4 S L23 AND 2001/SO
L25          11 S L23 AND 2000/SO
L26         107 S L22 NOT (L24 OR L25)

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L7              STR
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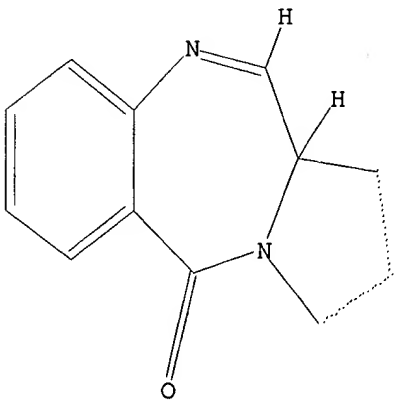

Structure attributes must be viewed using STN Express query preparation.
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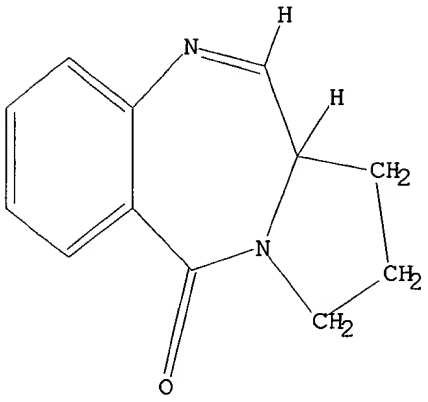
L13 HAS NO ANSWERS
L12 STR



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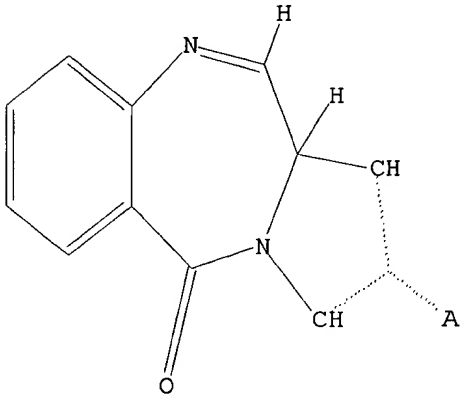
L14 STR



Structure attributes must be viewed using STN Express query preparation.

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L26 ANSWER 1 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 2000:161285 CAPLUS
DN 132:207852
TI Solid-phase preparation and combinatorial libraries of pyrrolobenzodiazepine derivatives for drug screening
IN Thurston, David Edwin; Howard, Philip Wilson
PA The University of Portsmouth Higher Education Corporation, UK
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012509	A2	20000309	WO 1999-GB2839	19990827
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9955262	A1	20000321	AU 1999-55262	19990827
	EP 1107970	A2	20010620	EP 1999-941767	19990827
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	GB 1998-18732	A	19980827		
	WO 1999-GB2839	W	19990827		

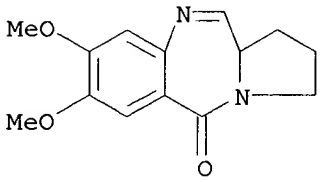
OS MARPAT 132:207852
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

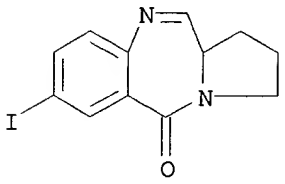
AB Title compds. I are prepd. [wherein: R = (un)substituted alk(en/yn)yl, aralkyl, aryl, or heteroat. analogs; R2 and R3 = H, R, OH, OR, O, :CHR, :CH2, CH2CO2R, CH2CO2H, CH2SO2R, OSO2R, CO2R, COR, and cyano; optionally double bond in ring; R6, R7, R8, and R9 = H, R, OH, OR, halo, NO2, amino, Me3Sn; or R7R8 = O(CH2)1-2O; R11 = H or R; Q = S, O, or NH; L = linking group or bond; Sup = solid support; or where 1 or more of R2, R3, R6, R7 and R8 = independently = H-(T)n-X-Y-A- where: X = CO, NH, S or O; T = combinatorial unit; Y = divalent group such that HY = R; A = O, S, NH, or bond; and n = pos. integer]. The compds. are intermediates for pyrrolobenzodiazepine derivs. II, which are claimed as being potentially useful for treatment of bacterial, parasitic, viral, and gene-based diseases. For example, the supported chloroformate ester III underwent (1) elaboration with 4,5-dimethoxyanthranilic acid, (2) amidation with 2-pyrrolidinemethanol, and (3) oxidative cyclization using SO3.pyridine and DMSO, to give the invention compd. IV. Photochem. cleavage of IV gave the corresponding aminal, which was dehydrated in situ to give the corresponding compd. V. The cleavage product showed cytotoxicity against human leukemia cells which was identical to that of authentic samples of V. Another compd. I was derivatized at a sidechain using 3 amino acids in

3 chain positions to give a 27-member combinatorial library.

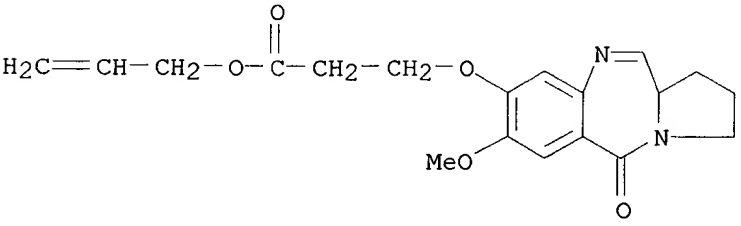
IT **260417-09-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; solid-phase prepn. and combinatorial libraries of pyrrolobenzodiazepine derivs. for drug screening)
RN 260417-09-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-dimethoxy- (9CI) (CA INDEX NAME)



IT **260417-05-8P 260417-31-0P 260417-36-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(target compd.; solid-phase prepn. and combinatorial libraries of pyrrolobenzodiazepine derivs. for drug screening)
RN 260417-05-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-iodo- (9CI) (CA INDEX NAME)

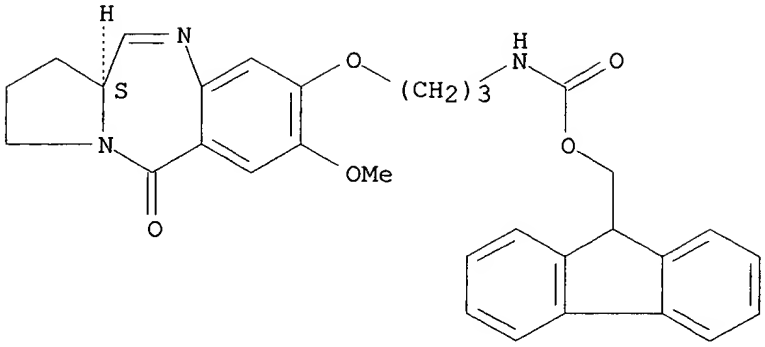


RN 260417-31-0 CAPLUS
CN Propanoic acid, 3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]-, 2-propenyl ester (9CI) (CA INDEX NAME)



RN 260417-36-5 CAPLUS
CN Carbamic acid, [3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



applicants

L26 ANSWER 2 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 2000:161284 CAPLUS
DN 132:207851
TI Preparation of pyrrolobenzodiazepines (PBDs) as antitumor agents
IN Thurston, David Edwin; Howard, Philip Wilson
PA The University of Portsmouth Higher Education Corporation, UK
SO PCT Int. Appl., 258 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012508	A2	20000309	WO 1999-GB2838	19990827
	WO 2000012508	A3	20000921		
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	EP 1109812	A2	20010627	EP 1999-943066	19990827
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	GB 1998-18733	A	19980827		
	GB 1999-1929	A	19990128		
	WO 1999-GB2838	W	19990827		

OS MARPAT 132:207851
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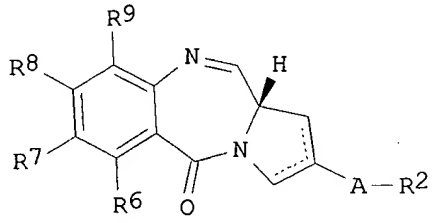

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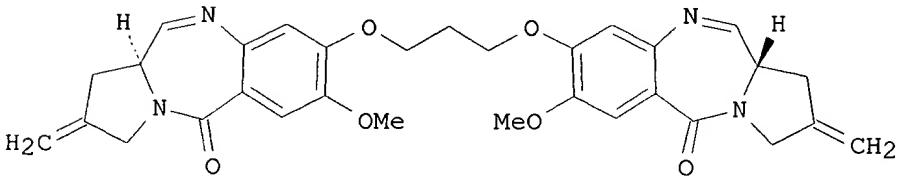


II

AB 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one derivs. (I) [wherein A = CH2 or a single bond; R = (un)substituted (ar)alkyl, (ar)alkenyl, or (ar)alkynyl;

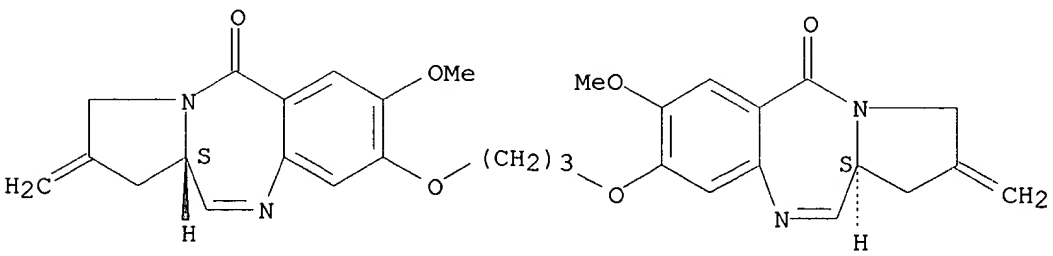
R2 = R, OH, OR, CO2H, CO2R, COH, COR, SO2R, CN; R6, R7, R8, and R9 = independently H, R, OH, OR, halo, NH2, NHR, NO2, SnMe3; or the compd. is a dimer with each monomer being the same or different and being of formula I and the R8 groups of the monomers form a -X-R'-X- bridge, where R' is an alkylene chain which may contain .gtoreq. 1 heteroatoms and/or arom. rings and/or carbon-carbon double or triple bonds, and each X = independently O, S, or N] were prepd. for the treatment of gene-based diseases, e.g. neoplastic diseases and Alzheimer's disease, and also bacterial, parasitic, and viral infections. For example, II was synthesized in a 6-step sequence. 1',3'-Bis(4-carboxy-2-methoxy-5-nitrophenoxy)propane (prepn. given) was bisamidated with (2S)-2-(tert-butyldimethylsilyloxymethyl)-4-methylenepyrrolidine (74%). TBAF-mediated cleavage of the silyl protecting groups (94%), followed by redn. of the nitro groups by NH2NH2 in the presence of Raney Ni (63%) and N-acylation with allyl chloroformate (50%), gave the protected diamine. Ring closure was accomplished under Swern oxidn. conditions, (COCl)2-DMSO and TEA, (32%). Finally, the imine was formed from the carbinolamine by N-deprotection using Pd(PPh3)4 and elimination of H2O (77%). Both large scale in vitro cytotoxicity cell screens and and in vivo hollow fiber and human tumor xenograft assays were performed on selected compds. of the invention. For instance, II exhibited potent and selective cytotoxicity against the lung cancer cell line NCI-H460, the colon cell line HCC-2998, the CNS cancer cell line SNB-75, and the melanoma cell lines MALME-3M (very potent, 0.08 .mu.M) and UACC-62 (very potent, 0.07 .mu.M). In human xenograft studies against five types of tumors, II demonstrated anticancer activity with mixed toxicity results. In addn., II was shown to be the most potent DNA-stabilizing agent known to date according to a DNA helix melting temp. assay. The IC50 value for II in the A2780 human ovarian carcinoma cell line was only 23 pM, a 320-fold increase in cytotoxicity compared to the known antitumor agent DSB-120 (IC50 = 5.2 nM). Remarkably, II was also almost 9000-fold more potent in the cisplatin-resistant A2780cisR cell line (IC50 = 24 pM) than DSB-120 (IC50 = 0.21 mM), suggesting that II may have potential in the treatment of cisplatin-refractory disease.

IT **232931-57-6P**, SJG 136
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of 5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one antitumor agents from 2-amino- or 2-nitrobenzoic acid derivs. and pyrrolidines)

RN 232931-57-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-2-methylene-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

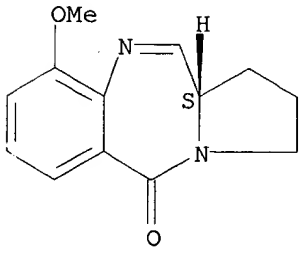
Absolute stereochemistry. Rotation (+).



IT **110715-89-4P**, AG 140 **133954-34-4P**, DRH 271
187083-51-8P, AG 105 **215723-10-7P**, UP 2026
219537-19-6P, AG 135 **260417-36-5P**, UP 2088
260417-62-7P 260417-63-8P 260417-64-9P
260543-36-0P, SB-A 67 **260543-52-0P**, SJG 245
260543-54-2P, SJG 301 **260543-56-4P**, SJG 303
260543-57-5P, AN-SJG **260543-81-5P**, KEC 570
260544-27-2P, UP 2089 **260546-05-2P**, BSD-SJG
260546-06-3P, SJG 244 **260546-07-4P**, MMY-SJG
260546-08-5P, UP 2067 **260546-09-6P**, DRH 165
260546-54-1P, DRH-NA 7 **260546-58-5P**, DRH 69
260546-76-7P, DRH 168 **260546-91-6P**, AG 150
260546-93-8P, DRH 105 **260546-94-9P**, UP 2028
260546-96-1P, UP 2005 **260546-97-2P**, UP 2006
260546-99-4P, UP 2007 **260547-00-0P**, UP 2008
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of 5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one antitumor agents from 2-amino- or 2-nitrobenzoic acid derivs. and pyrrolidines)

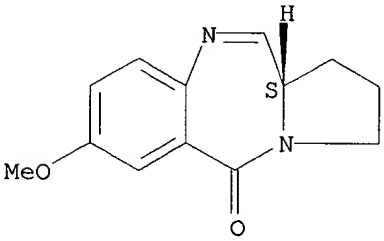
RN 110715-89-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 133954-34-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

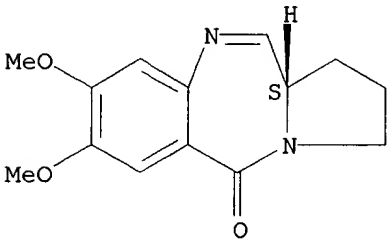
Absolute stereochemistry.



RN 187083-51-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-

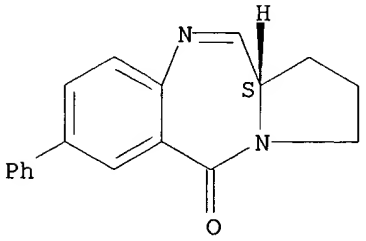
dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



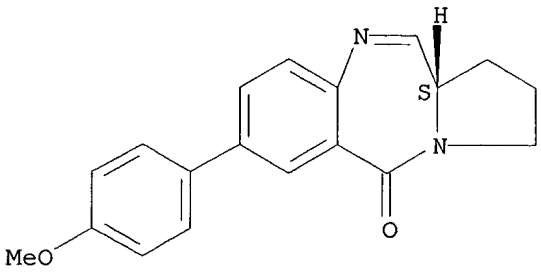
RN 215723-10-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-phenyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



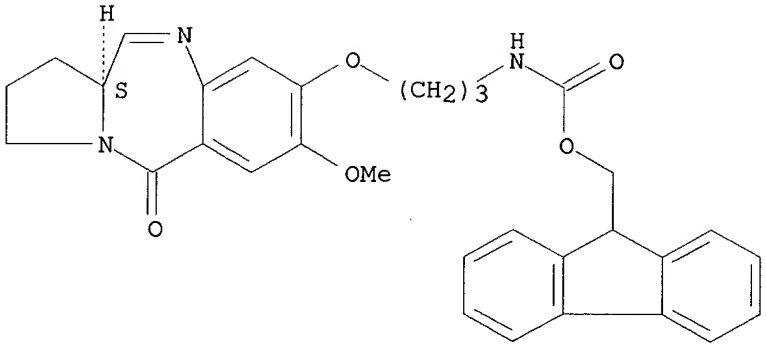
RN 219537-19-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(4-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



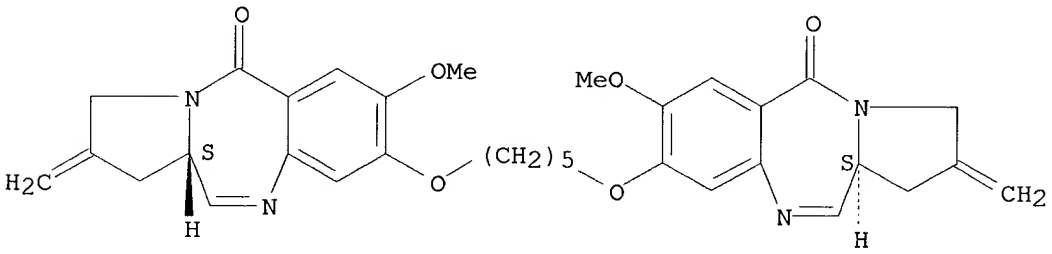
RN 260417-36-5 CAPLUS
CN Carbamic acid, [3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



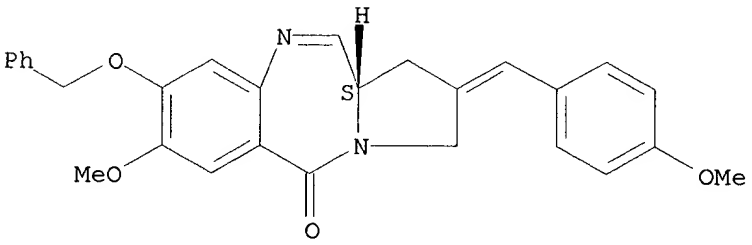
RN 260417-62-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-2-methylene-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



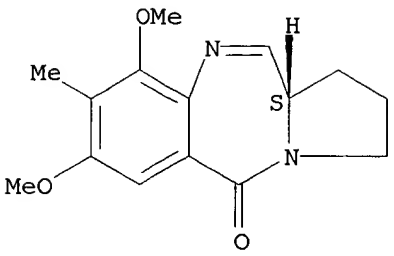
RN 260417-63-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-2-[(4-methoxyphenyl)methylene]-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



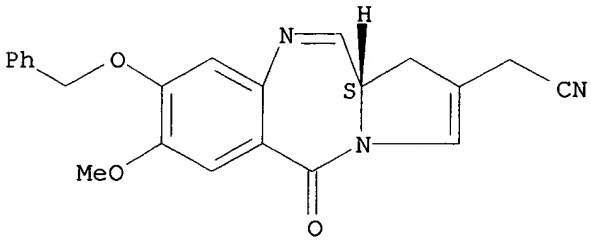
RN 260417-64-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,9-dimethoxy-8-methyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



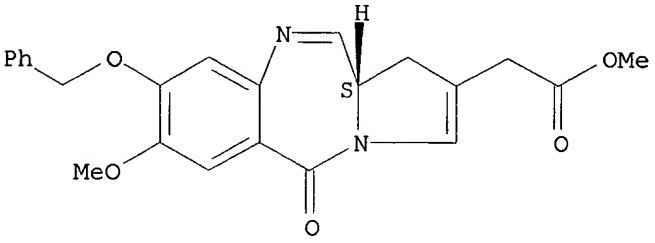
RN 260543-36-0 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acetonitrile, 5,11a-dihydro-7-methoxy-5-oxo-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



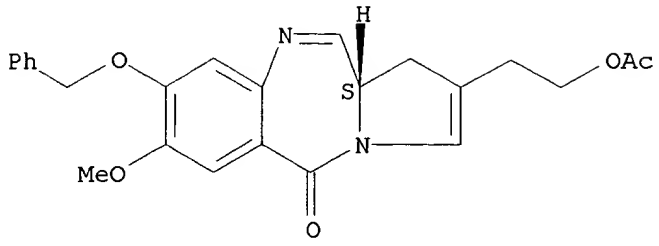
RN 260543-52-0 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acetic acid, 5,11a-dihydro-7-methoxy-5-oxo-8-(phenylmethoxy)-, methyl ester, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



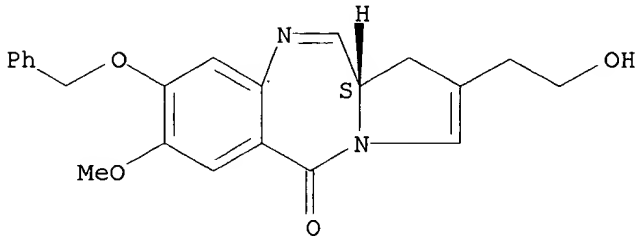
RN 260543-54-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-[2-(acetyloxy)ethyl]-1,11a-dihydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



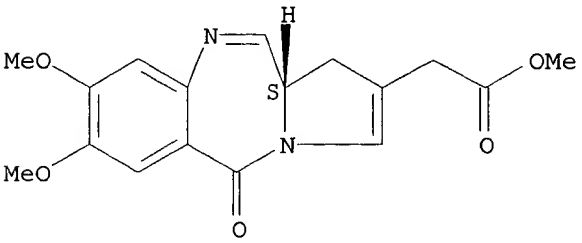
RN 260543-56-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-2-(2-hydroxyethyl)-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 260543-57-5 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acetic acid, 5,11a-dihydro-7,8-dimethoxy-5-oxo-, methyl ester, (11aS)- (9CI) (CA INDEX NAME)

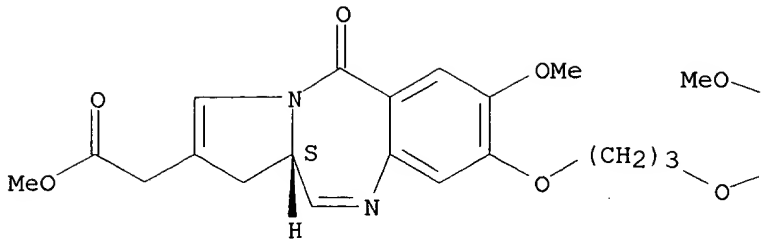
Absolute stereochemistry.



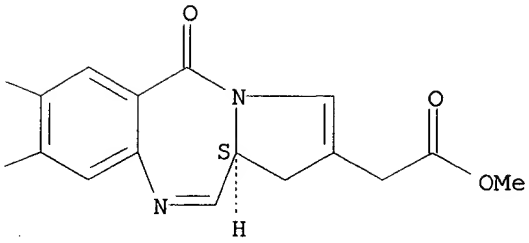
RN 260543-81-5 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acetic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[5,11a-dihydro-7-methoxy-5-oxo-, dimethyl ester, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

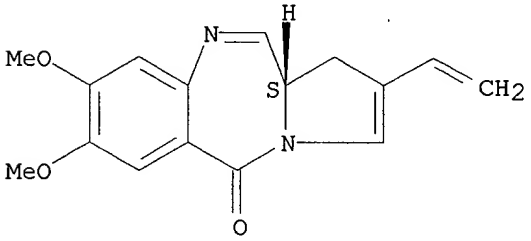


PAGE 1-B



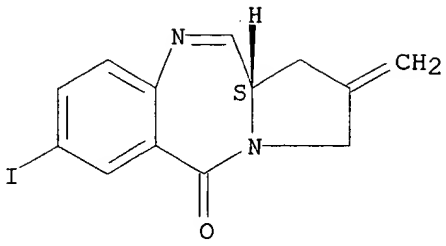
RN 260544-27-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethenyl-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



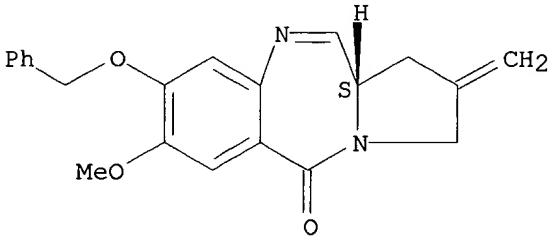
RN 260546-05-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-iodo-2-methylene-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



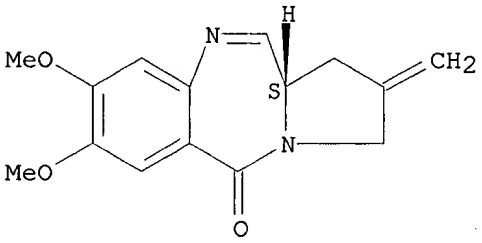
RN 260546-06-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-2-methylene-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



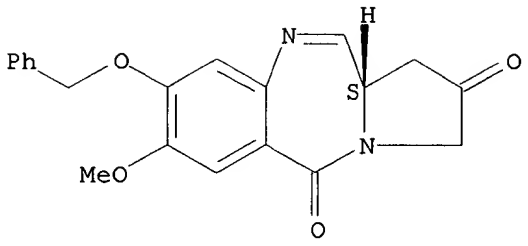
RN 260546-07-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-dimethoxy-2-methylene-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



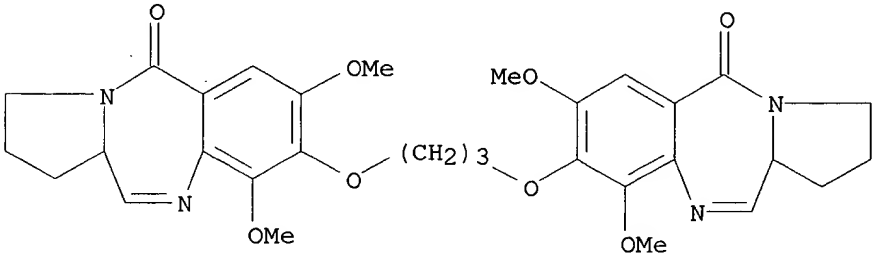
RN 260546-08-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H)-dione, 1,11a-dihydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



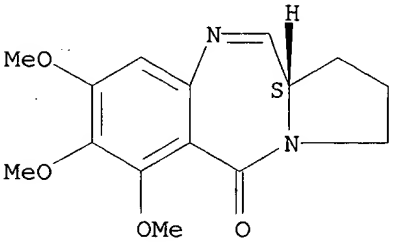
RN 260546-09-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7,9-dimethoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



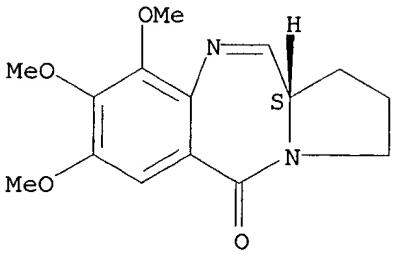
RN 260546-54-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-6,7,8-trimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



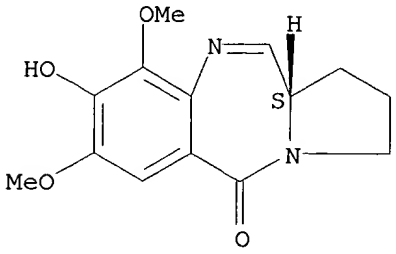
RN 260546-58-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8,9-trimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



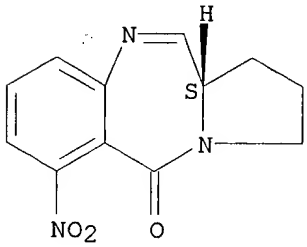
RN 260546-76-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7,9-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



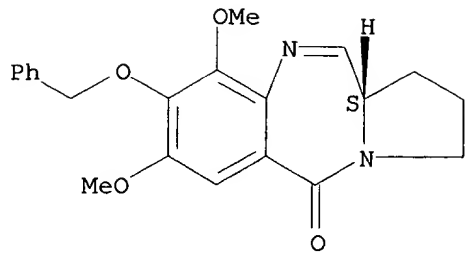
RN 260546-91-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-6-nitro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



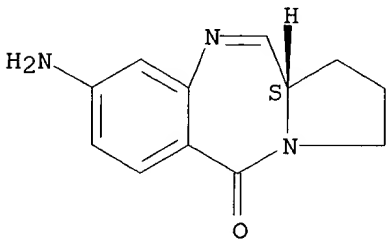
RN 260546-93-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,9-dimethoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



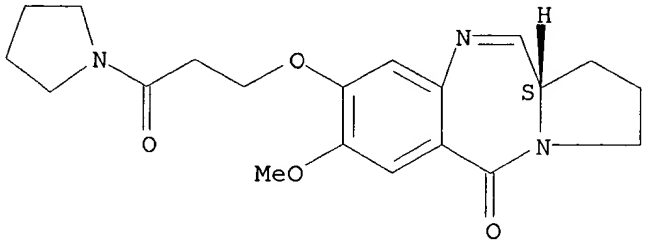
RN 260546-94-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8-amino-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



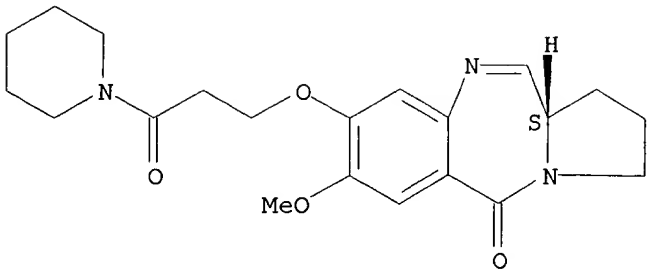
RN 260546-96-1 CAPLUS
CN Pyrrolidine, 1-[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



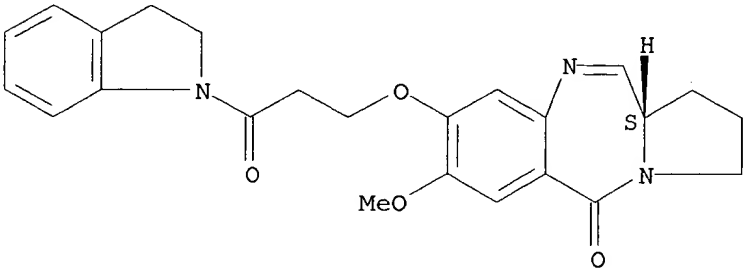
RN 260546-97-2 CAPLUS
CN Piperidine, 1-[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



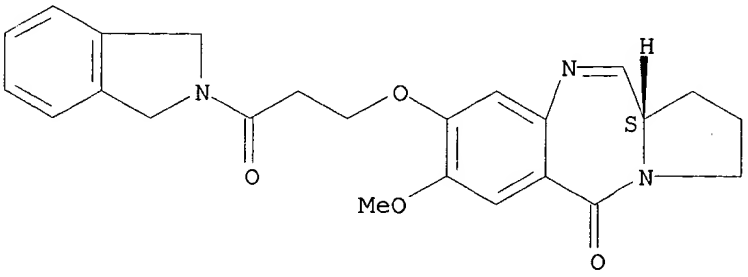
RN 260546-99-4 CAPLUS
CN 1H-Indole, 2,3-dihydro-1-[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 260547-00-0 CAPLUS
CN 1H-Isoindole, 2,3-dihydro-2-[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 3 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 2000:161283 CAPLUS
DN 132:207703
TI Preparation of pyrrolobenzodiazepines (PBDs) as antitumor antibiotics
IN Thurston, David Edwin; Howard, Philip Wilson
PA The University of Portsmouth Higher Education Corporation, UK
SO PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012507	A2	20000309	WO 1999-GB2837	19990827
	WO 2000012507	A3	20000831		
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OS MARPAT 132:207703
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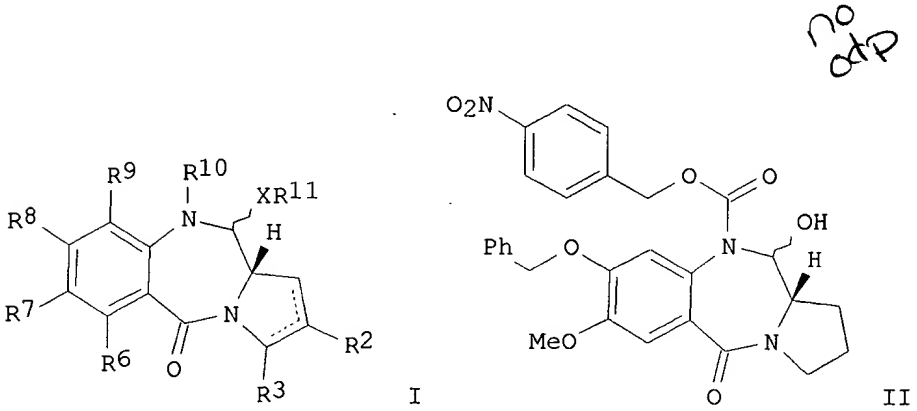


I II

AB 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one derivs. (I) [wherein R = (un)substituted (ar)alkyl, etc.; R2 and R3 = independently H, R, OH, OR, =O, =CH-R, =CH2, CH2-CO2R, CH2-CO2H, CH2-SO2R, O-SO2-R, CO2R, COR, or CN; R6, R7, R8, and R9 = independently H, R, OH, OR, halo, NH2, NO2, or Me3Sn; or R7 and R8 together form a -O-(CH2)p-O- group, where p = 1 or 2; or the compd. is a dimer with each monomer being the same or different and being of formula I and the R8 groups of the monomers form a -T-R'-T- bridge, where R' is an alkylene chain which may contain .gtoreq. 1 heteroatoms

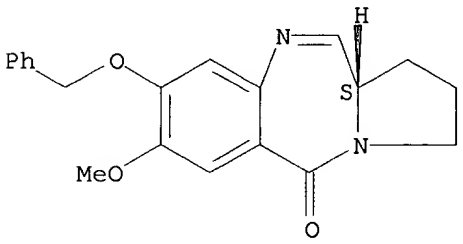
and/or arom. rings and/or carbon-carbon double or triple bonds, and each T = independently O, S, or N; R10 = a therapeutically removable N-protecting group; R11 = H or R; X is S, O, or NH] were prepd. for the treatment of cancer and other site-specific diseases where a local increase of toxicity is beneficial to the patient. Examples include the syntheses of benzyl DC-81, benzyl tomaymycin, and DSB-120 prodrugs starting from 2-nitrobenzoic acid derivs. and pyrrolidines. Data from enzyme and light activation studies and cytotoxicity assays are also given. For example, the nitroreductase-activated benzyl DC-81 (II) was formed in a 6-step sequence involving: (1) benzylation of vanillic acid (67%); (2) ring nitration (82%); (3) amidation with (2S)-pyrrolidinemethanol (88%); (4) redn. of the nitro group (81%); (5) N-addn. of 4-nitrobenzyl chloroformate; and (6) cyclization using Swern oxidn. conditions (31%). In the presence of nitroreductase and the NADH co-factor, II demonstrated antitumor activity (IC50 = 1-5 .mu.M) against the SW1116 and LS174T human adenocarcinoma colonic cell lines. II proved non-toxic in SW1116 cells at concns. .ltoreq. 500 .mu.M and showed slight toxicity in LS174T cells at concns. > 100 .mu.M. I may also be suitable for treating bacterial, parasitic, or viral infections by exploiting a unique enzyme produced at the site of infection which is not natural to the host, or by exploiting an elevation in the amt. of an enzyme which does occur naturally in the host.

IT **127810-79-1**, Benzyl DC 81 **140676-21-7**, DSB 120
187083-51-8, UP 2025
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of pyrrolobenzodiazepinone prodrugs from 2-nitrobenzoic acid derivs. and pyrrolidines for the treatment of cancer)

RN 127810-79-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

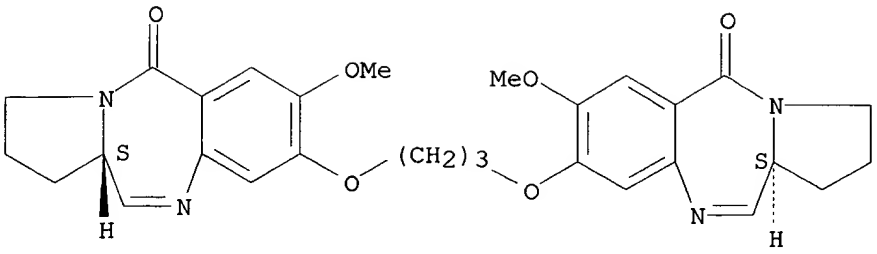
Absolute stereochemistry. Rotation (+).



RN 140676-21-7 CAPLUS

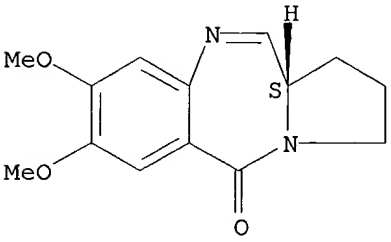
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 187083-51-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 4 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 2000:161282 CAPLUS
DN 132:208134
TI Preparation of peptidyl pyrrolobenzodiazepines as pharmaceuticals
IN Thurston, David Edwin; Howard, Philip Wilson
PA The University of Portsmouth Higher Education Corporation, UK
SO PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012506	A2	20000309	WO 1999-GB2836	19990827
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	EP 1107969	A2	20010620	EP 1999-941765	19990827
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	WO 1999-GB2836	W	19990827		

OS MARPAT 132:208134
GI

no odP

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Benzodiazepines I [X = CO2H, NH2 or protected amino, SH, OH; A = O, S, NH, or a single bond; R2, R3 = H, R, OH, OR, :O, :CHR, :CH2, CH2CO2R, CH2CO2H, CH2SO2R, OSO2R, CO2R, COR, CN, where R = alkyl, alkenyl, alkynyl, aralkyl, (un)substituted aryl; there is optionally a double bond between C1 and C2 or C2 and C3; R6, R7, R9 = H, R, OH, OR, halo, nitro, amino, Me3Sn; R11 = H or R; Q = S, O or NH; R10 is a nitrogen-protecting group; Y is a divalent group such that HY = R] were prepd. and incorporated into peptides for use as pharmaceuticals. Thus, pyrrolo[2,1-c][1,4]benzodiazepine deriv. II (Fmoc = fluorenylmethoxycarbonyl) was prepd. and applied to the synthesis of a 27-member glycine/valine/phenylalanine tripeptide library which was screened for inhibition of leukemia cells.

IT **260449-68-1P 260449-69-2P 260449-70-5P**
260449-71-6P 260449-72-7P 260449-73-8P
260449-74-9P 260449-75-0P 260449-76-1P
260449-77-2P 260449-78-3P 260449-79-4P
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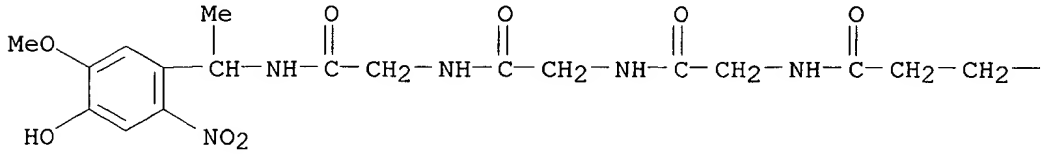
260450-34-8P 260450-36-0P 260450-38-2P
260450-40-6P 260450-41-7P 260450-43-9P
260450-45-1P 260450-47-3P 260450-49-5P
260450-51-9P 260450-53-1P 260450-54-2P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptidyl pyrrolobenzodiazepines as pharmaceuticals)

RN 260449-68-1 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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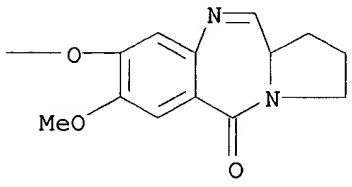
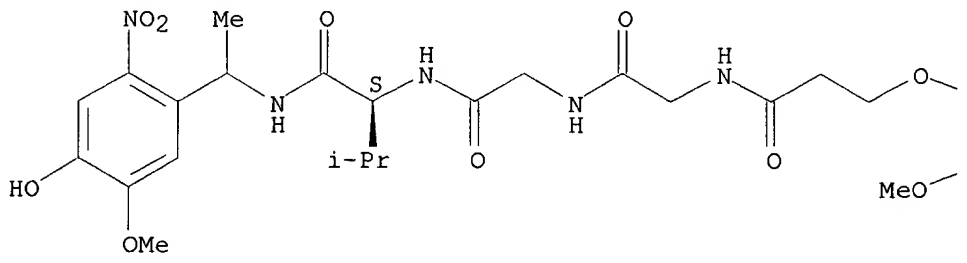


RN 260449-69-2 CAPLUS

CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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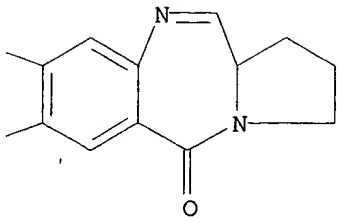
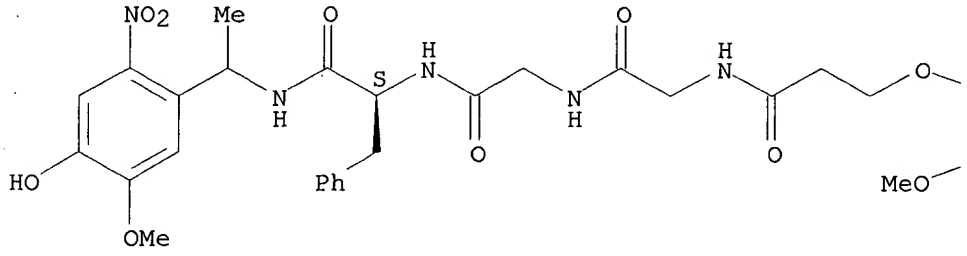


RN 260449-70-5 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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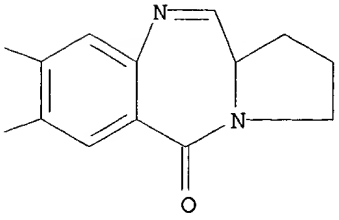
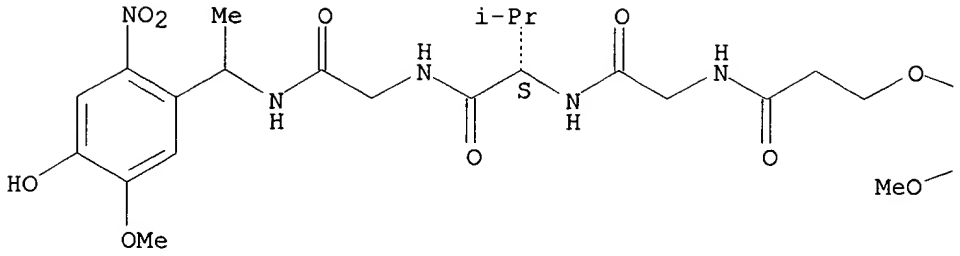


RN 260449-71-6 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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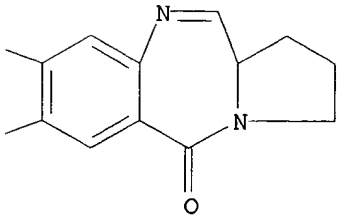
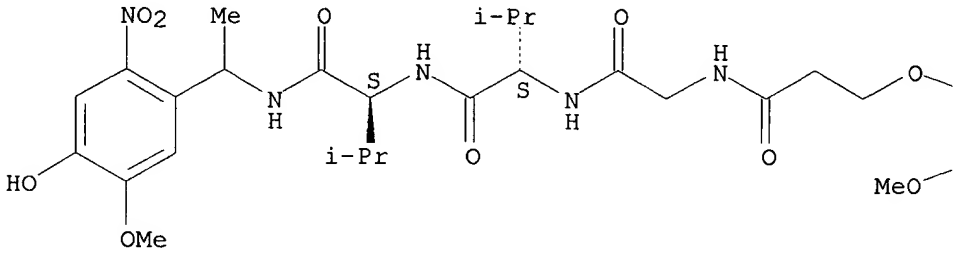


RN 260449-72-7 CAPLUS
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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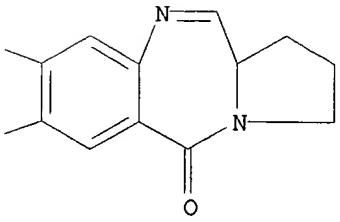
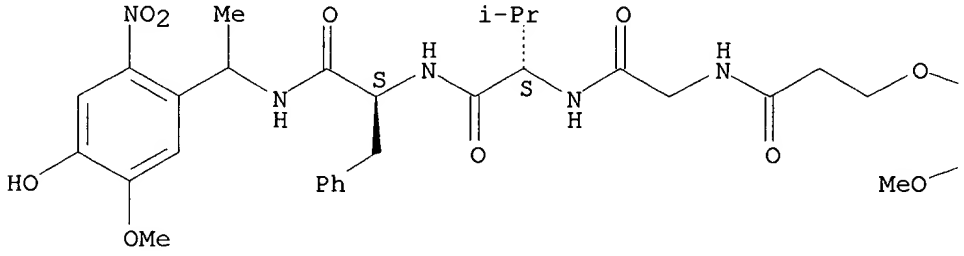


RN 260449-73-8 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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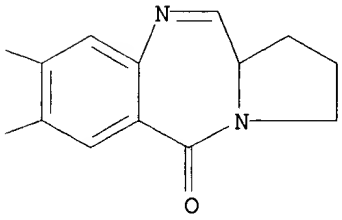
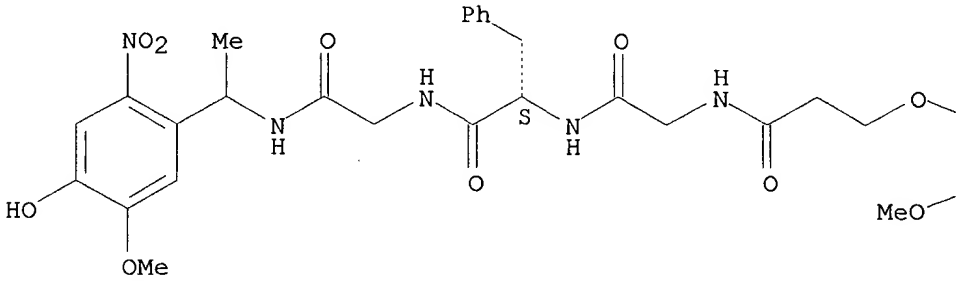


RN 260449-74-9 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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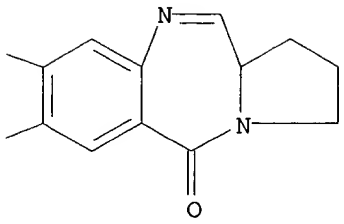
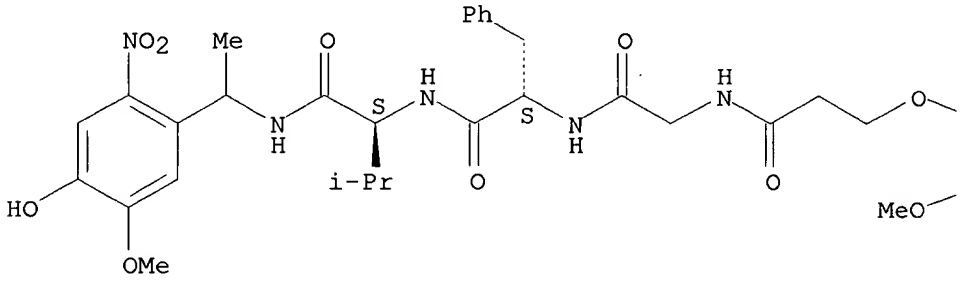


RN 260449-75-0 CAPLUS
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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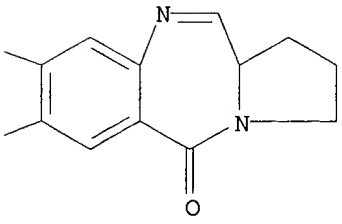
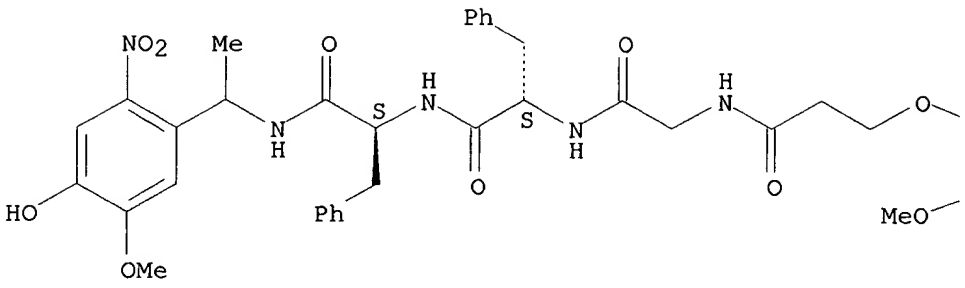


RN 260449-76-1 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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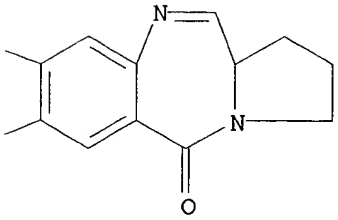
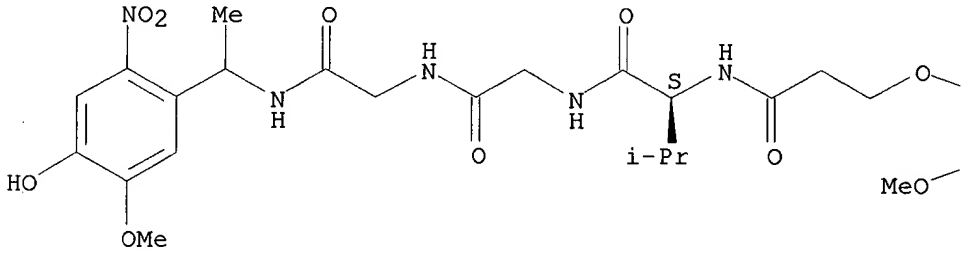


RN 260449-77-2 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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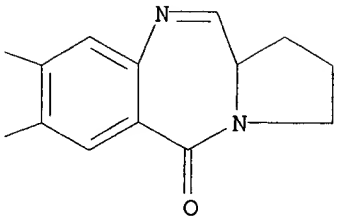
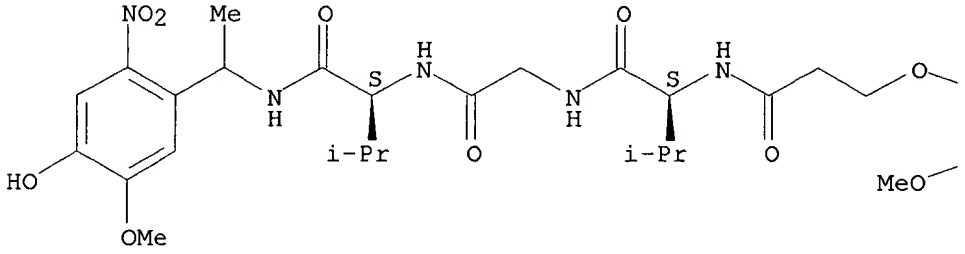


RN 260449-78-3 CAPLUS
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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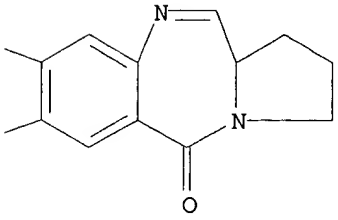
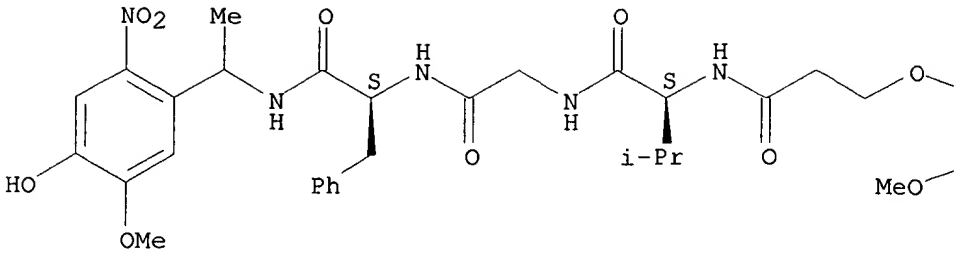


RN 260449-79-4 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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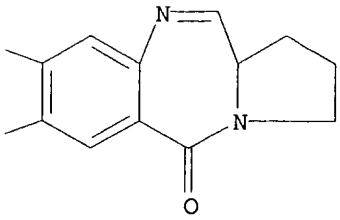
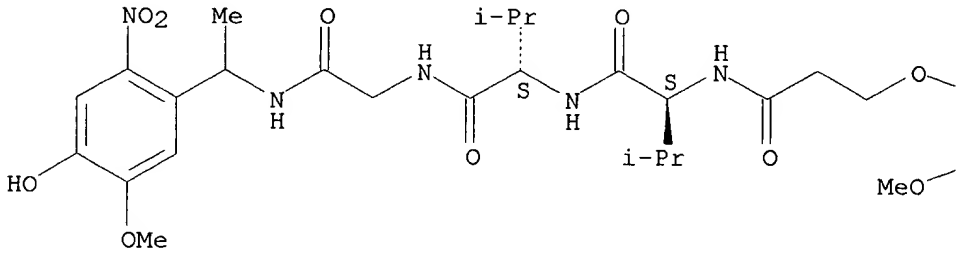


RN 260449-80-7 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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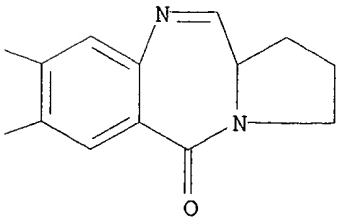
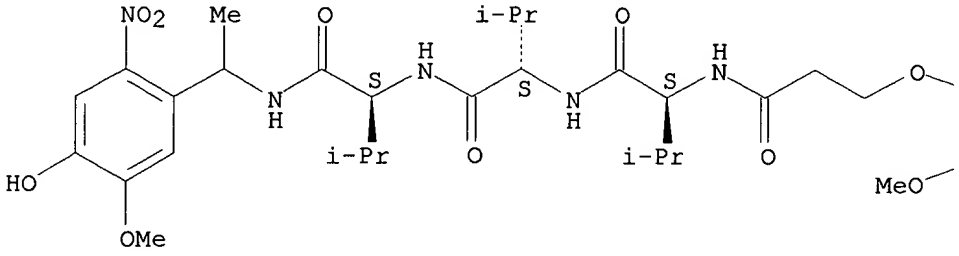


RN 260449-81-8 CAPLUS
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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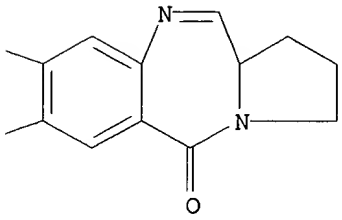
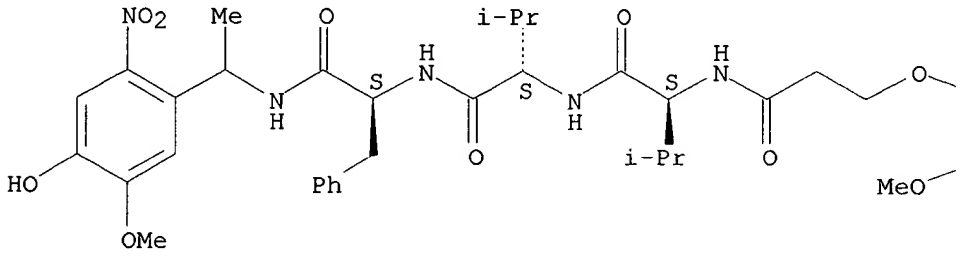


RN 260449-82-9 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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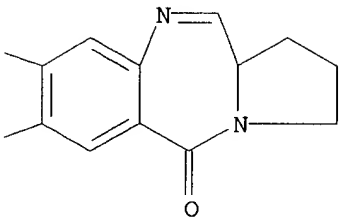
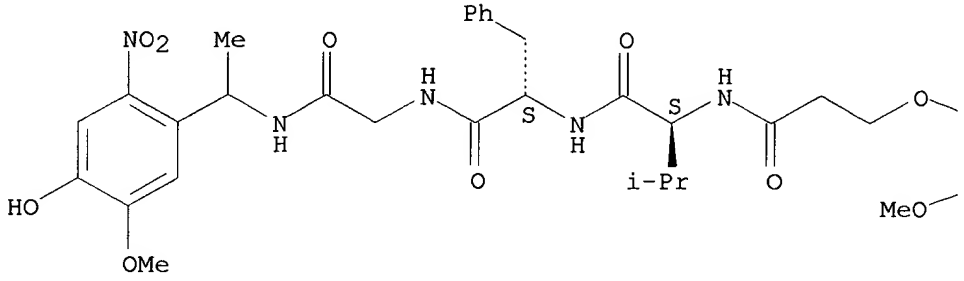


RN 260449-83-0 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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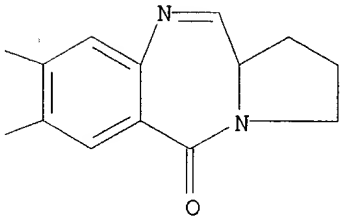
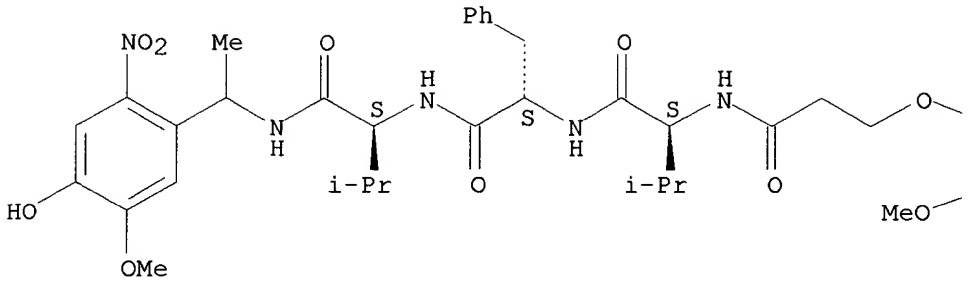


RN 260449-84-1 CAPLUS
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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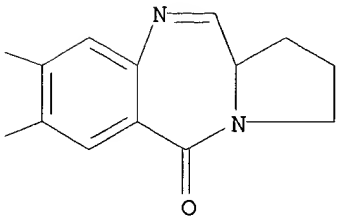
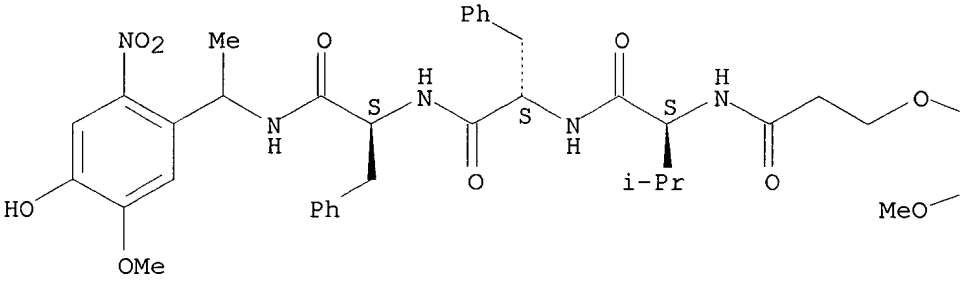


RN 260449-85-2 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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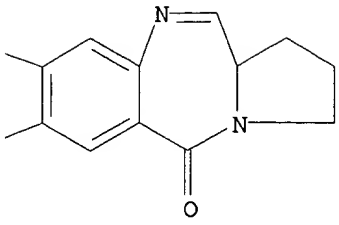
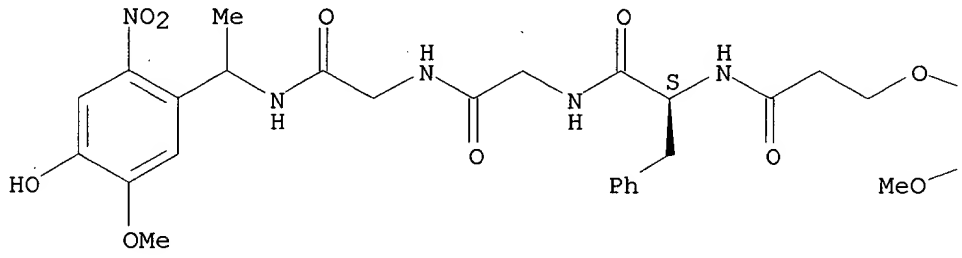


RN 260449-86-3 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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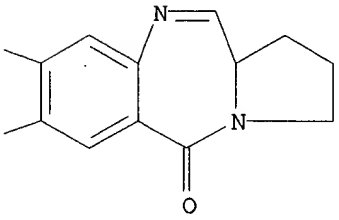
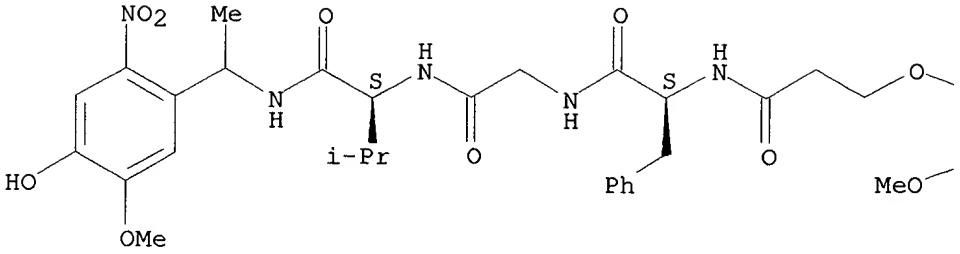


RN 260449-88-5 CAPLUS
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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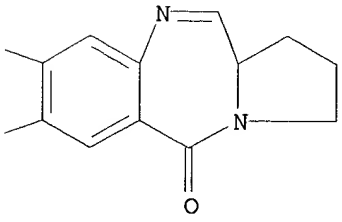

RN 260449-90-9 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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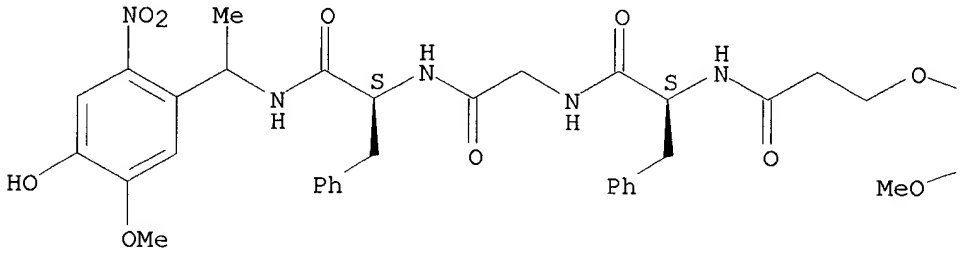

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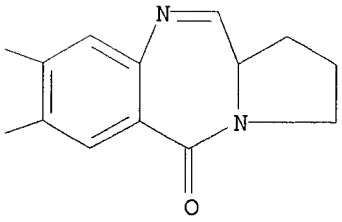

RN 260449-92-1 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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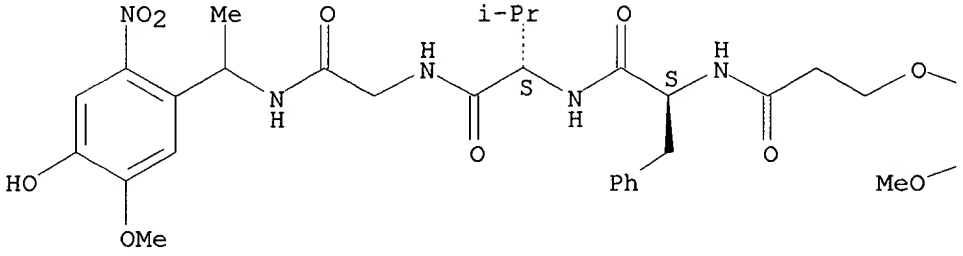

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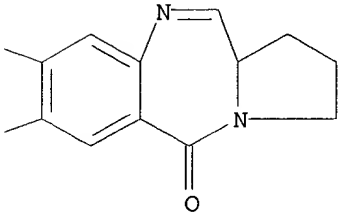

RN 260449-94-3 CAPLUS
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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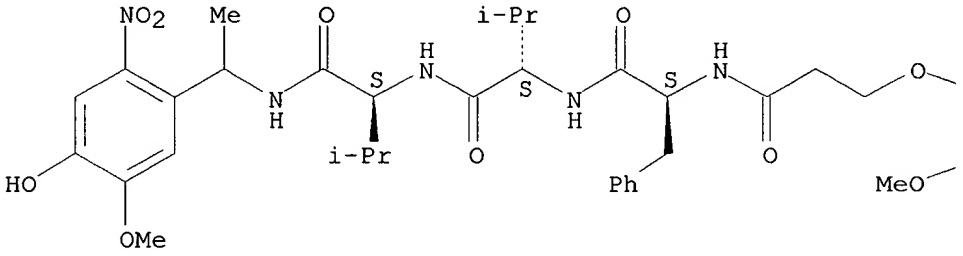

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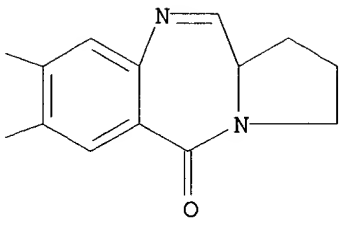
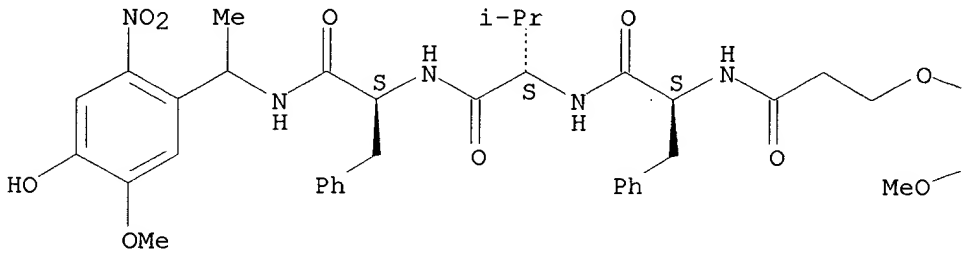


RN 260449-96-5 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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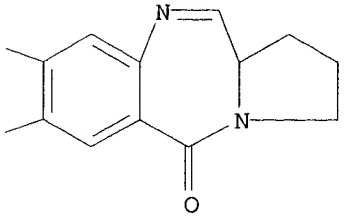

RN 260449-98-7 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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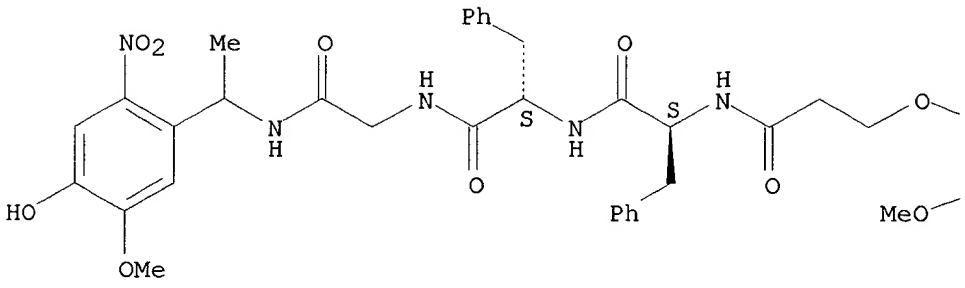

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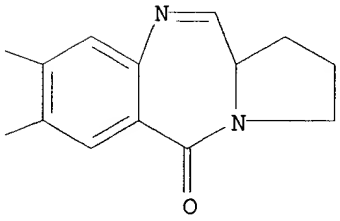

RN 260450-00-8 CAPLUS

CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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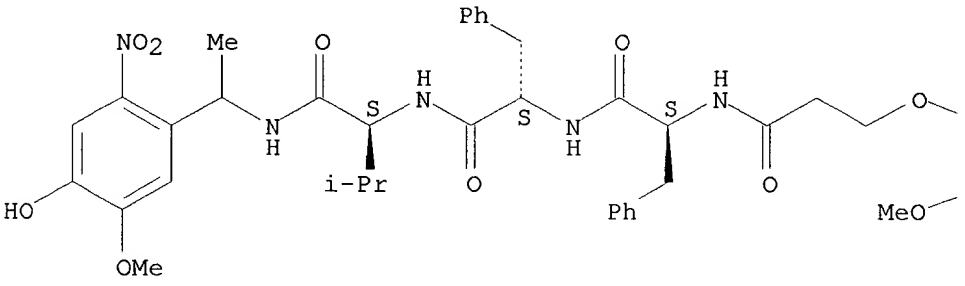

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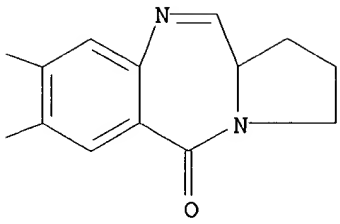

RN 260450-02-0 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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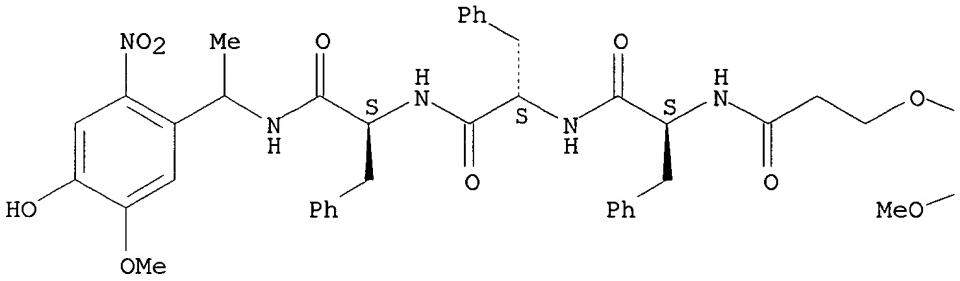

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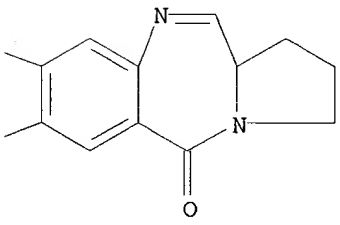

RN 260450-04-2 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

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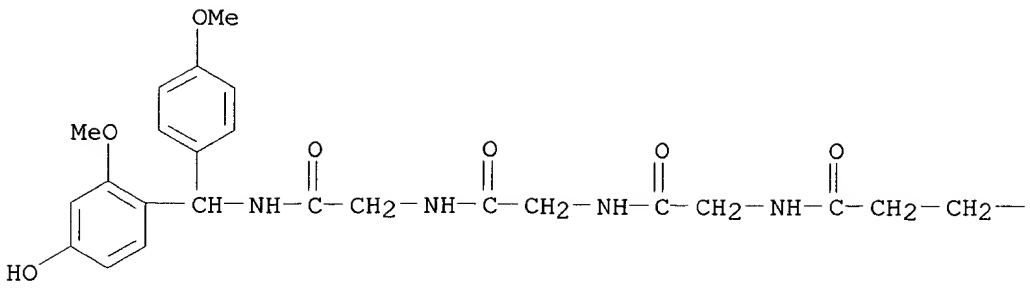

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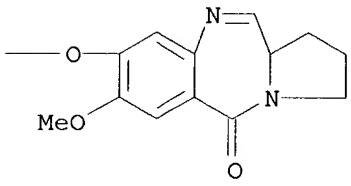

RN 260450-06-4 CAPLUS
CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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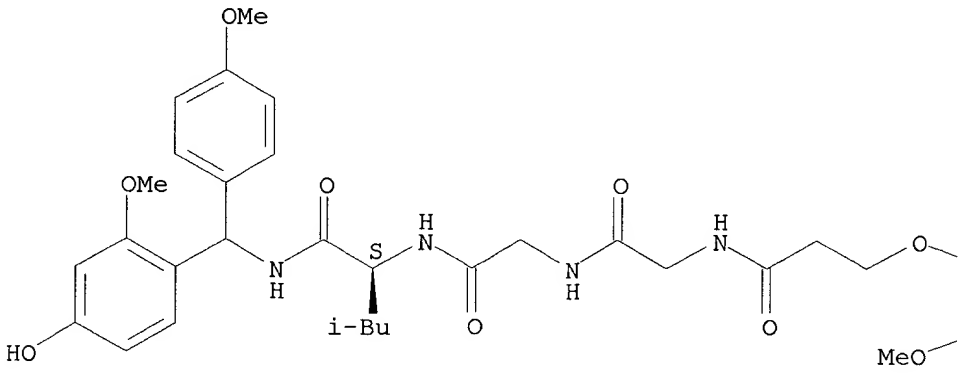

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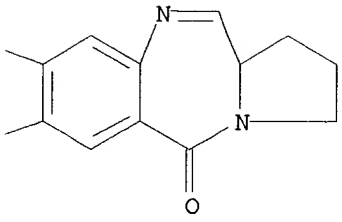

RN 260450-08-6 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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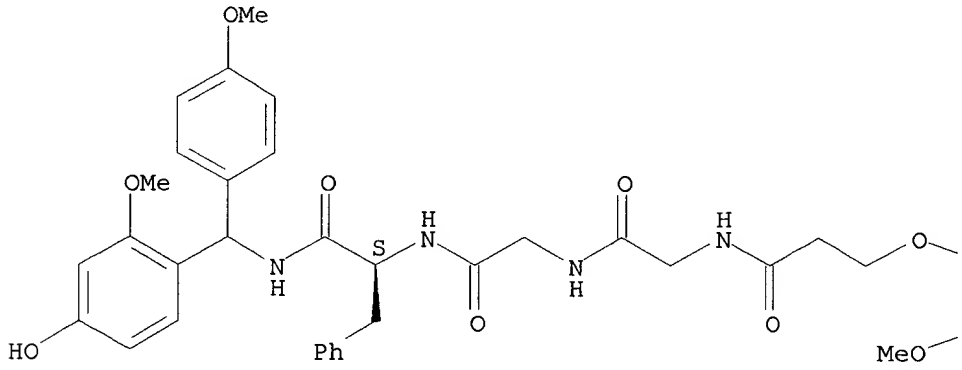

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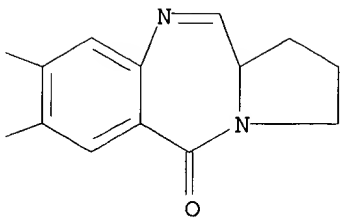

RN 260450-10-0 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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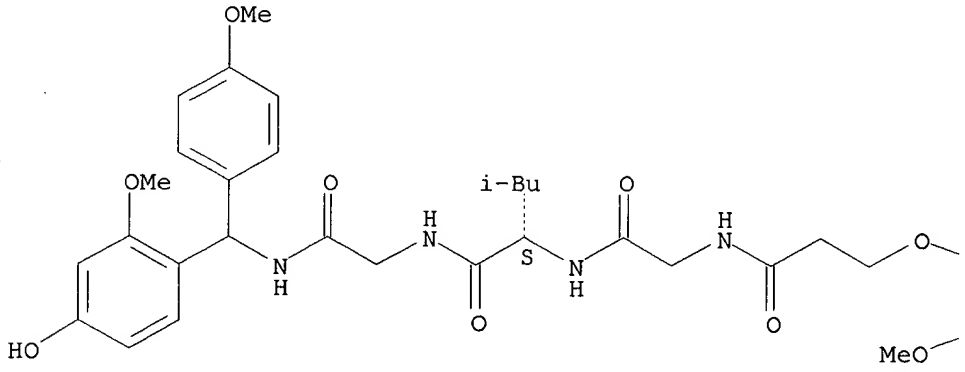

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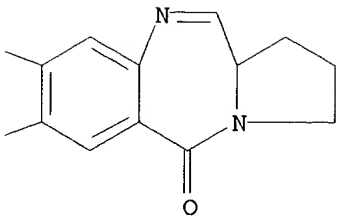

RN 260450-12-2 CAPLUS
CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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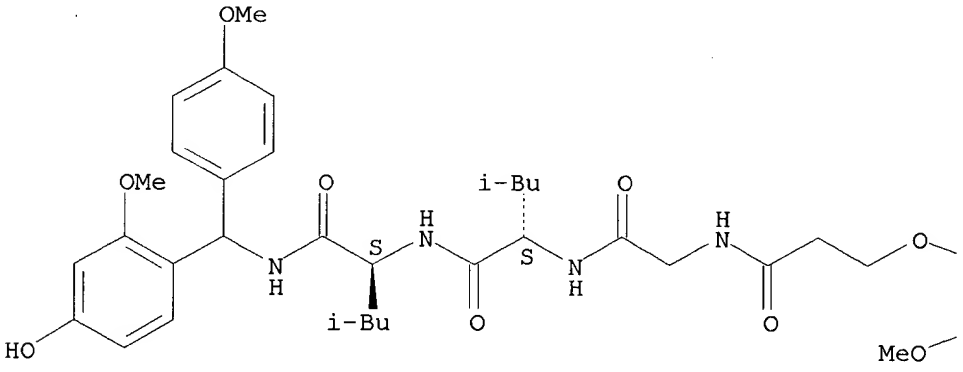

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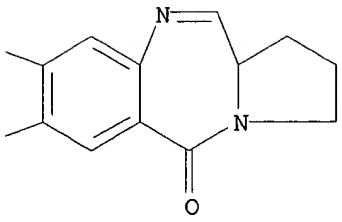

RN 260450-14-4 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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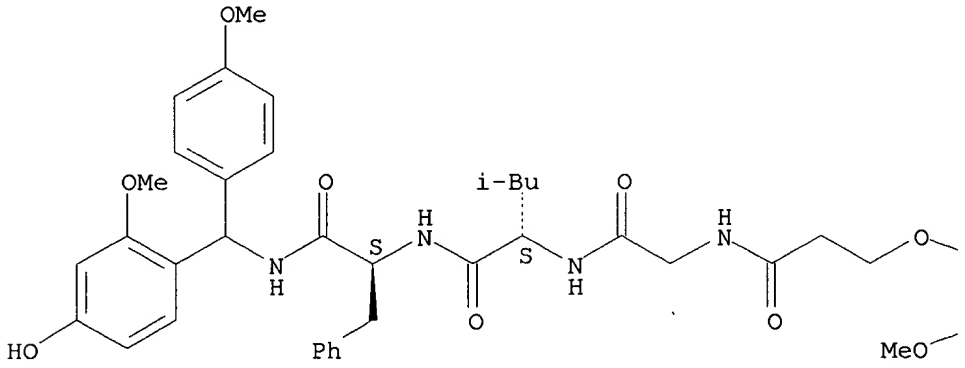

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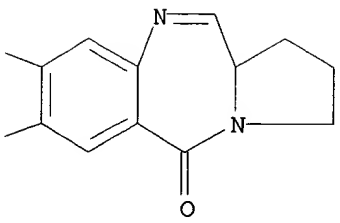

RN 260450-16-6 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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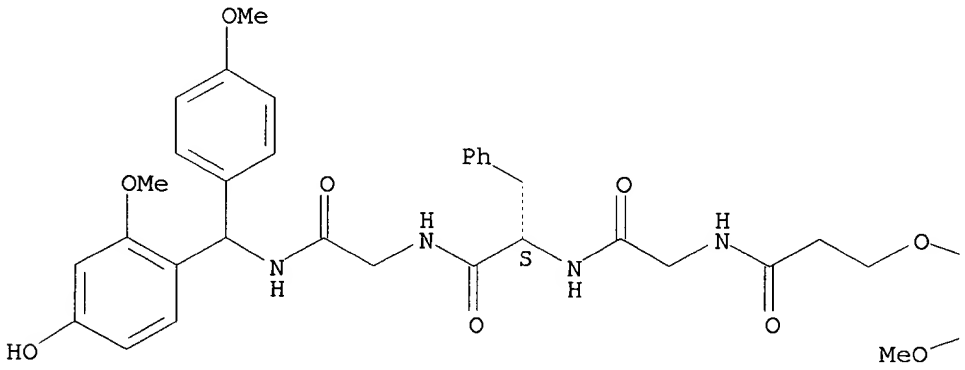

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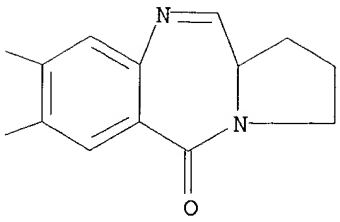

RN 260450-18-8 CAPLUS
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Absolute stereochemistry.

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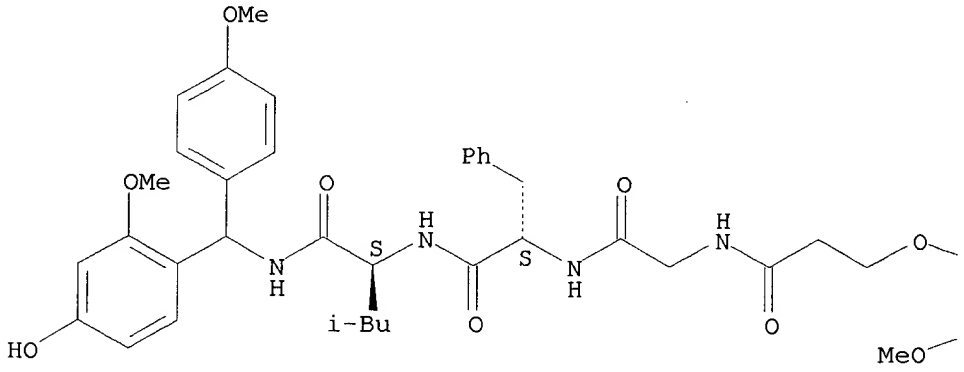

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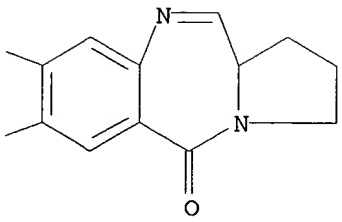

RN 260450-20-2 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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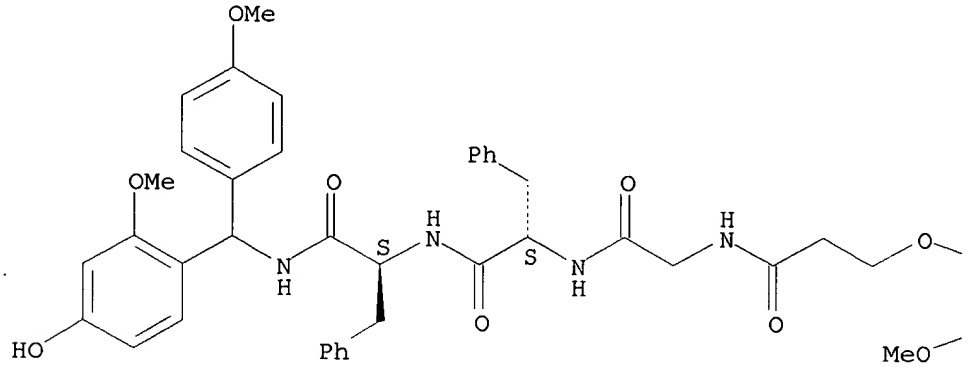

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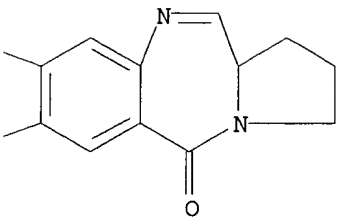
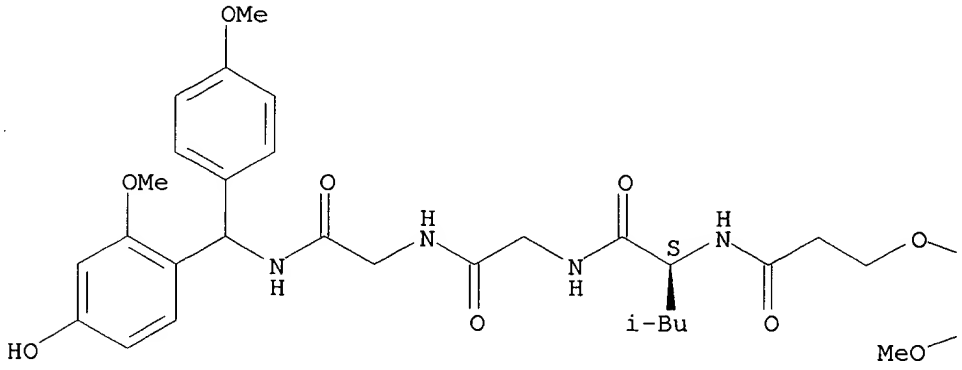


RN 260450-22-4 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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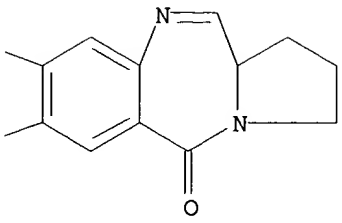
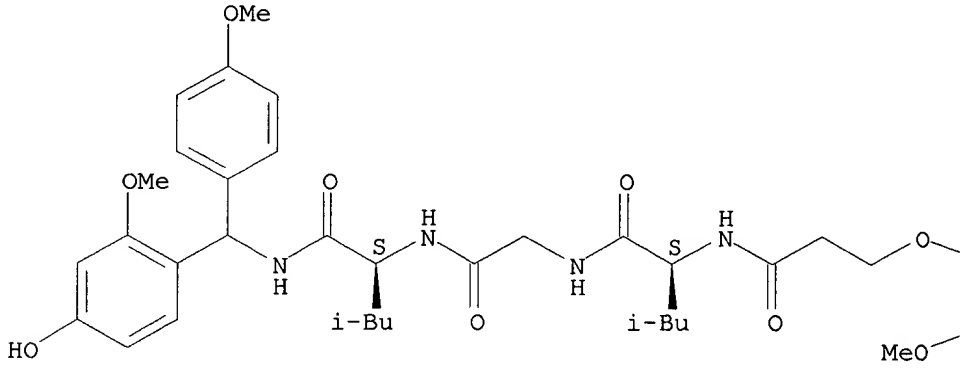


RN 260450-24-6 CAPLUS
CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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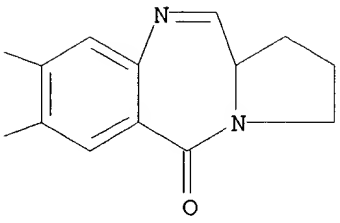
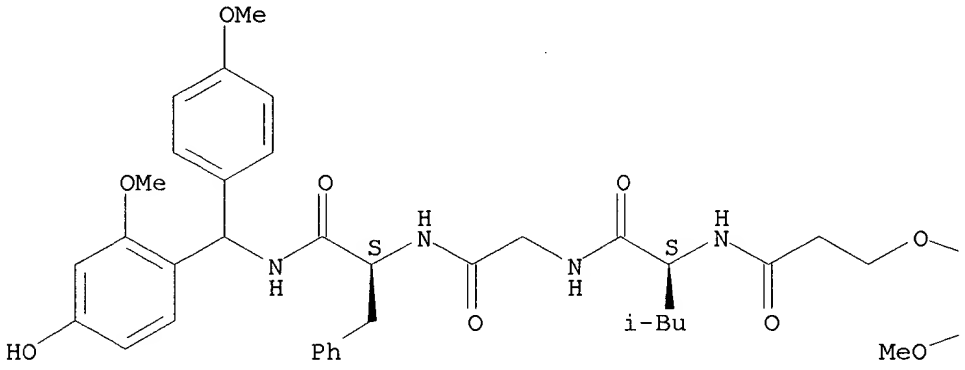


RN 260450-26-8 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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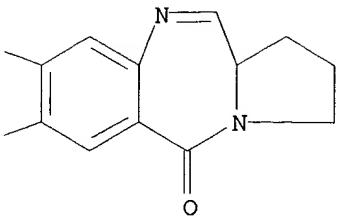
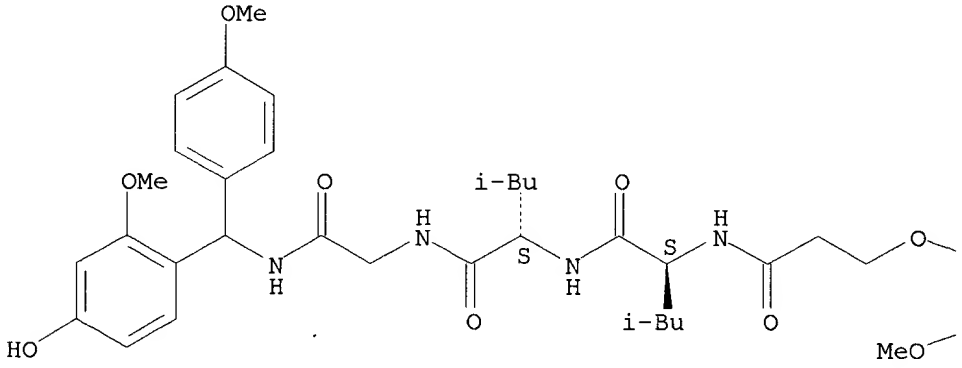


RN 260450-28-0 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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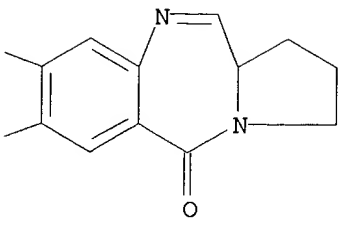
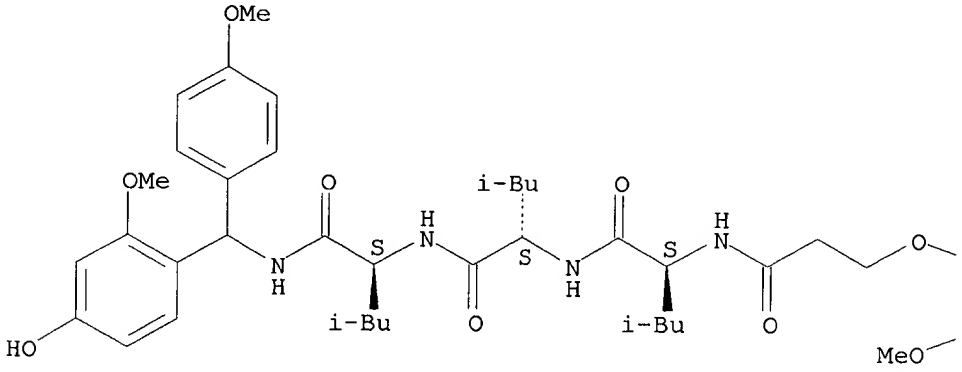


RN 260450-30-4 CAPLUS
CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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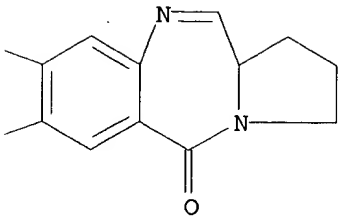
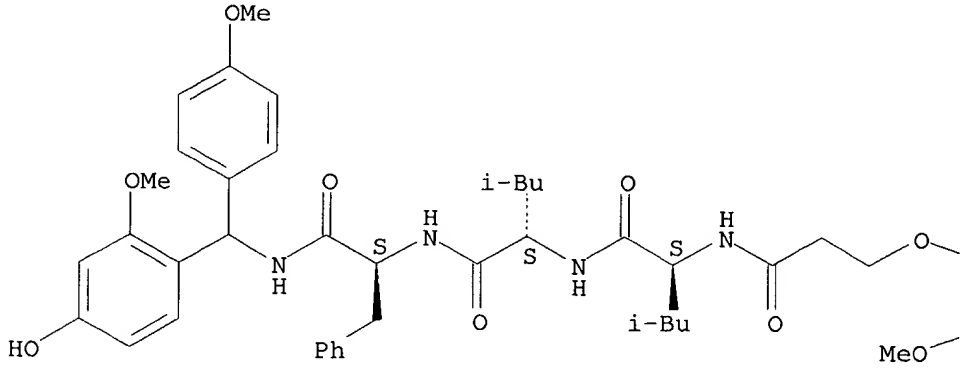


RN 260450-32-6 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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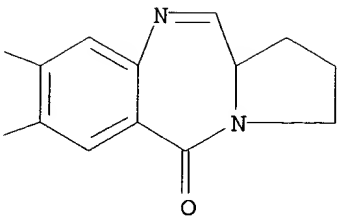
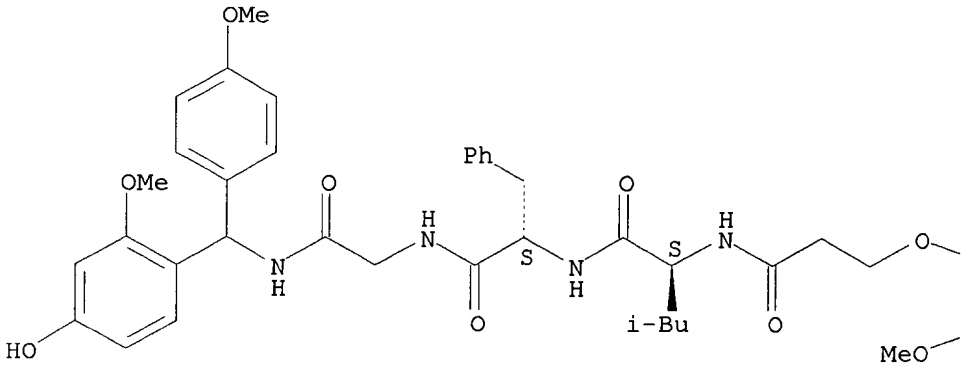


RN 260450-34-8 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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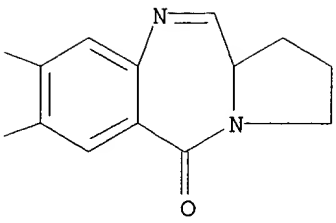
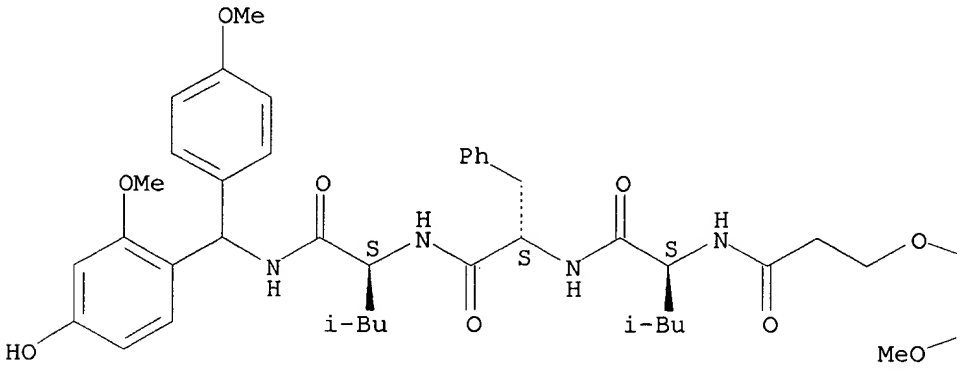


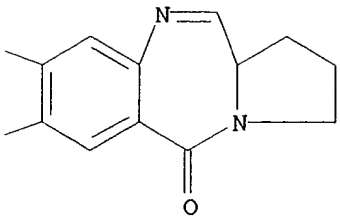
RN 260450-36-0 CAPLUS
CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



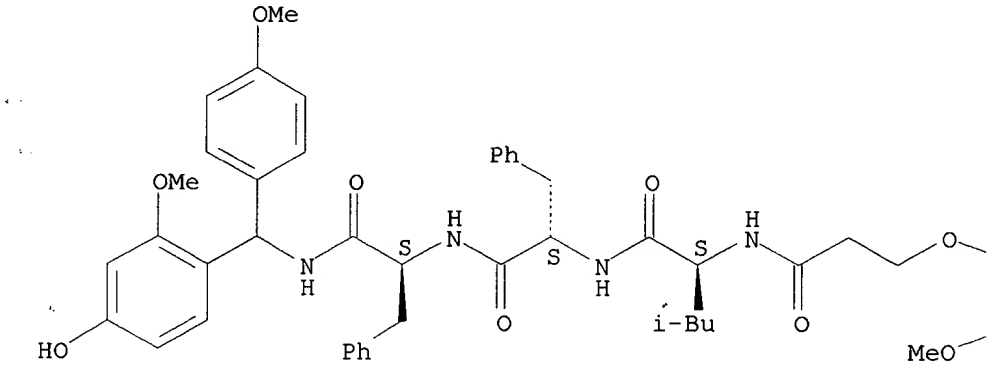
PAGE 1-B



RN 260450-38-2 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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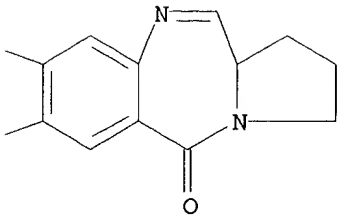
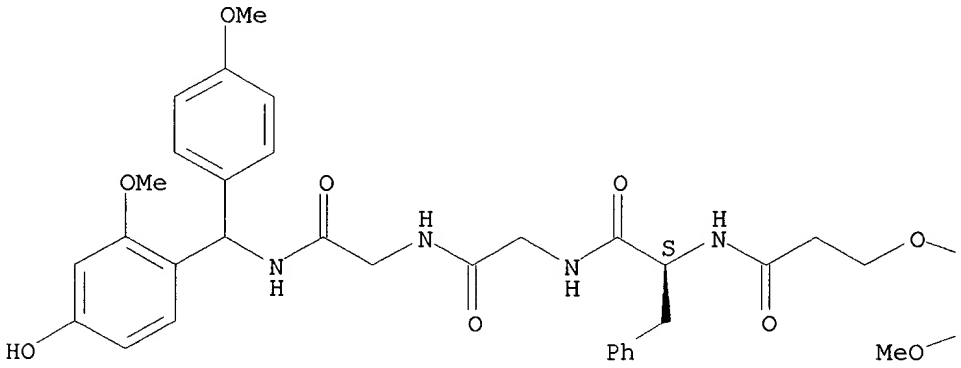


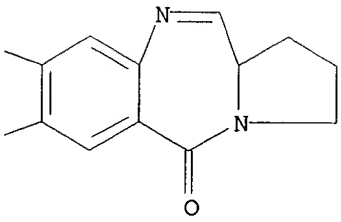
RN 260450-40-6 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



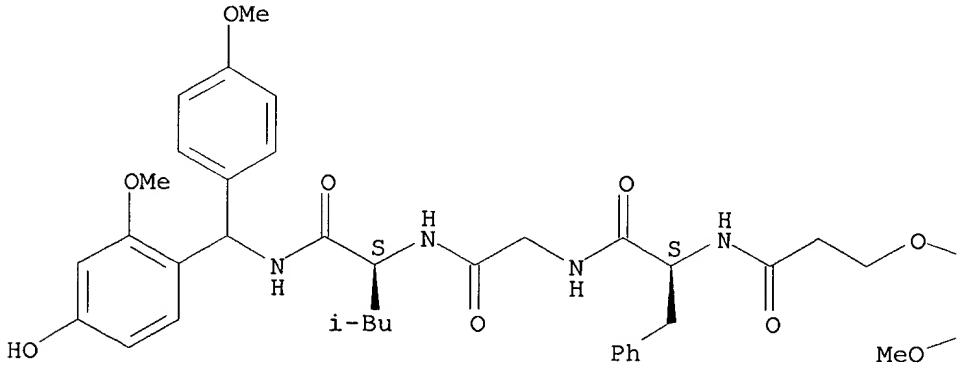
PAGE 1-B



RN 260450-41-7 CAPLUS
CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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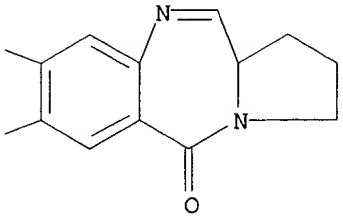
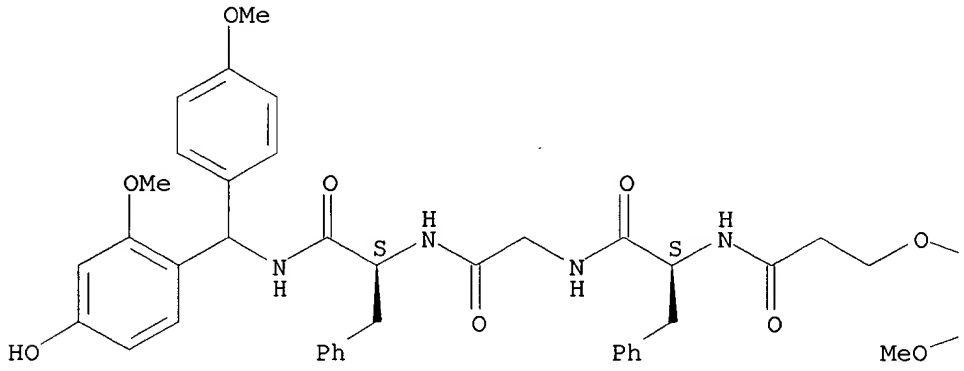


RN 260450-43-9 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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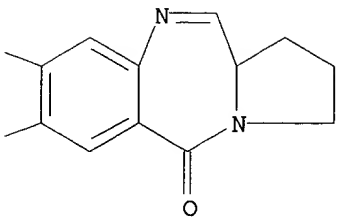
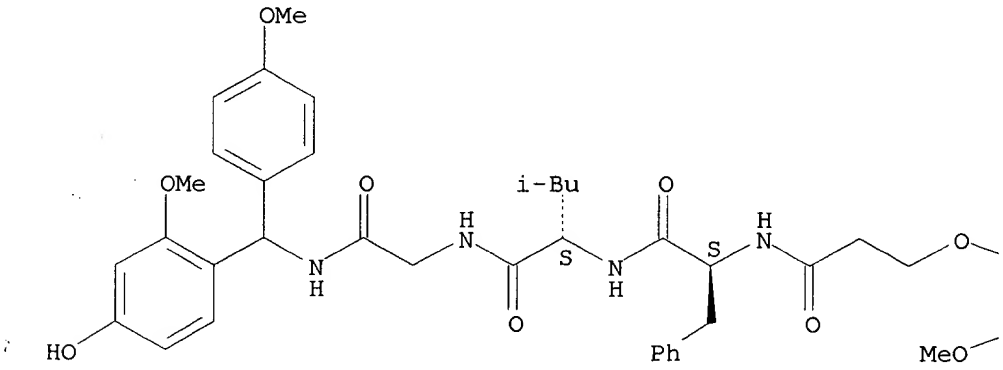


RN 260450-45-1 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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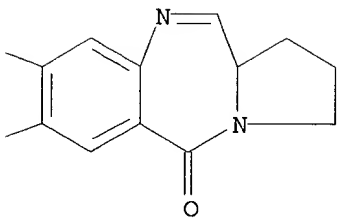
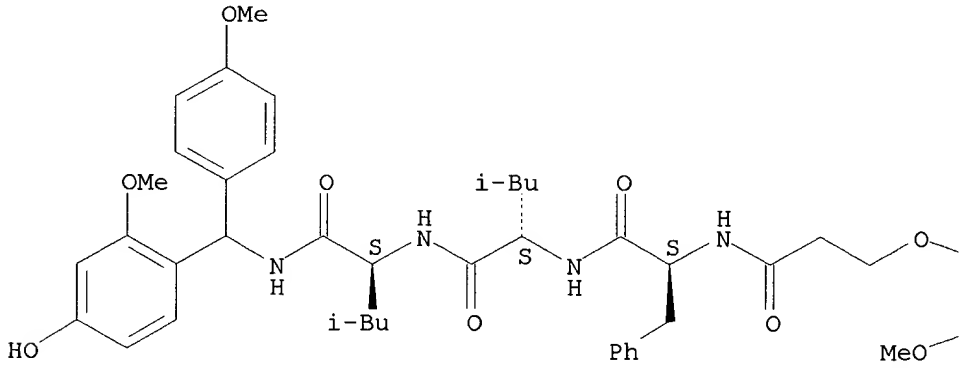


RN 260450-47-3 CAPLUS
CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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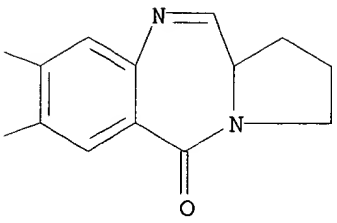
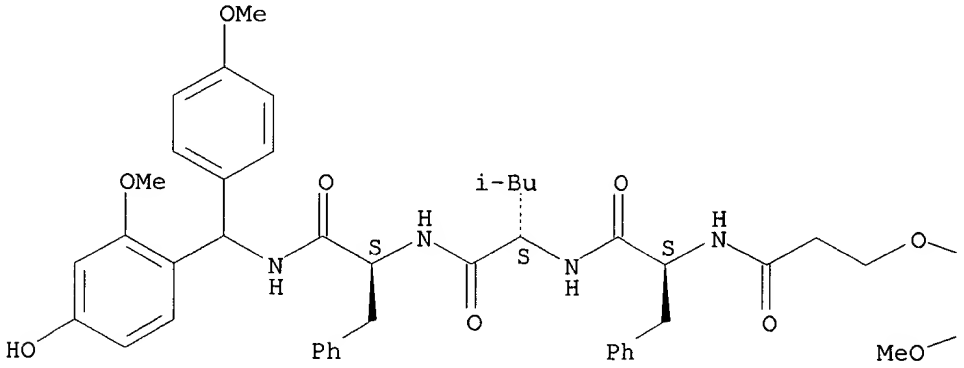


RN 260450-49-5 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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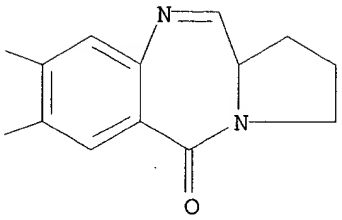
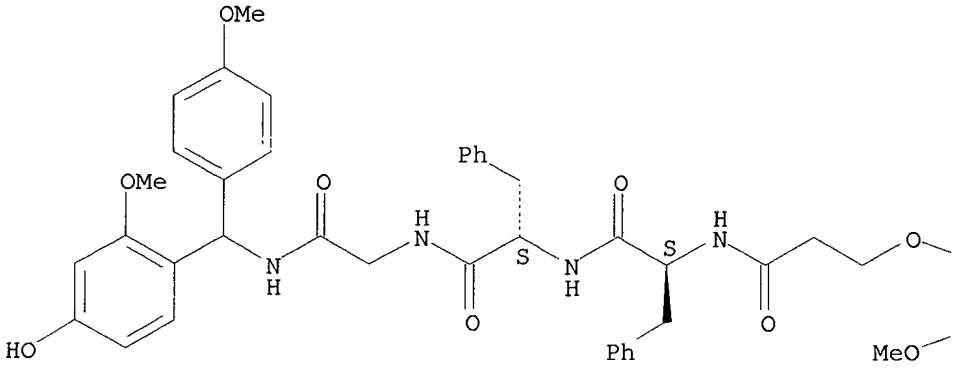


RN 260450-51-9 CAPLUS
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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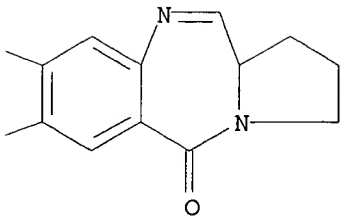
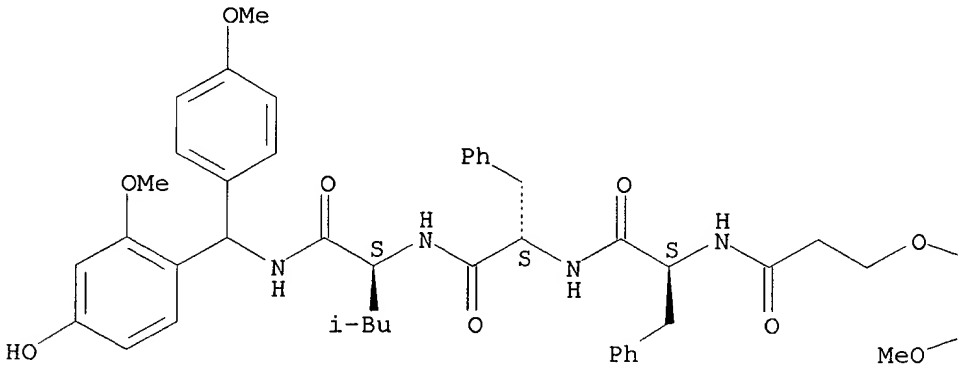


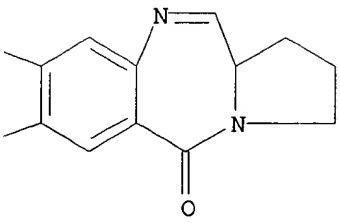
RN 260450-53-1 CAPLUS
CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



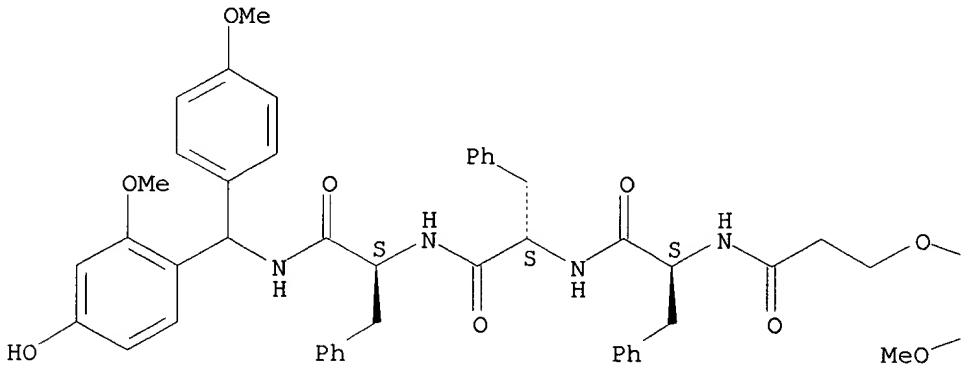
PAGE 1-B

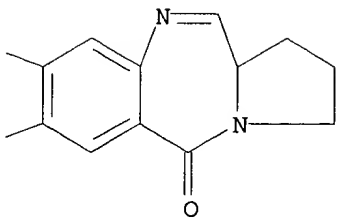


RN 260450-54-2 CAPLUS
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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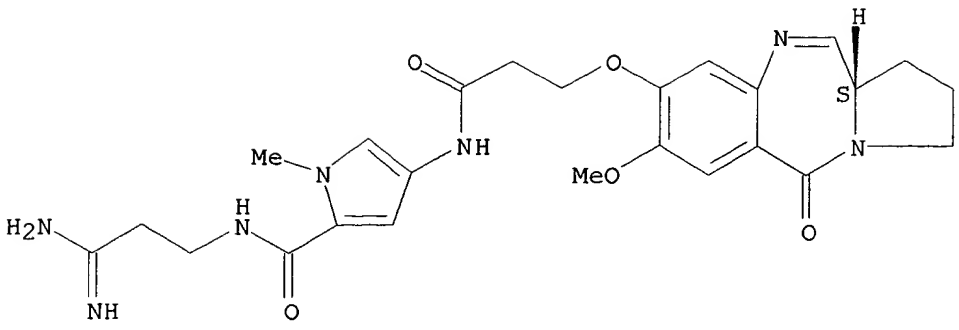
L26 ANSWER 5 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:758546 CAPLUS
DN 132:137361
TI Synthesis, in Vitro Antiproliferative Activity, and DNA-Binding Properties of Hybrid Molecules Containing Pyrrolo[2,1-c][1,4]benzodiazepine and Minor-Groove-Binding Oligopyrrole Carriers
AU Baraldi, Pier Giovanni; Balboni, Gianfranco; Cacciari, Barbara; Guiotto, Andrea; Manfredini, Stefano; Romagnoli, Romeo; Spalluto, Giampiero; Thurston, David E.; Howard, Philip W.; Bianchi, Nicoletta; Rutigliano, Cristina; Mischiati, Carlo; Gambari, Roberto
CS Dipartimento di Scienze Farmaceutiche e Dipartimento di Biochimica e Biologia Molecolare, Universita di Ferrara, Ferrara, 44100, Italy
SO J. Med. Chem. (1999), 42(25), 5131-5141
CODEN: JMCMAR; ISSN: 0022-2623 Dec
PB American Chemical Society
DT Journal
LA English
OS CASREACT 132:137361
AB The synthesis, biol. activity, and DNA-binding properties of a series of four pyrrolo[2,1-c][1,4]benzodiazepine (PBD) hybrids contg. polypyrrole side chains are described and structure-activity relationships examd. To investigate sequence selectivity and stability of drug/DNA complexes, DNase I footprinting and arrested polymerase chain reaction (PCR) were performed on human c-myc oncogene, estrogen receptor gene, and human immunodeficiency virus type 1 long terminal repeat (HIV-1 LTR) gene sequences. The antiproliferative activity of the hybrids was tested in vitro on human myeloid leukemia K562 and T-lymphoid Jurkat cell lines and compared to antiproliferative effects of the natural product distamycin A 1, its tetrapyrrole homolog, DC 81, and a PBD ester. The new hybrids exhibit different DNA-binding activity with respect to both distamycin A 1 and the parent PBD. In addn., a direct relationship was found between the no. of pyrrole rings present in the hybrids and the stability of drug/DNA complexes. With respect to antiproliferative effects, it was found that the increase in the length of the polypyrrole backbone leads to an increase of in vitro antiproliferative effects, i.e., the hybrid with 4 pyrroles is more active than the other ones both against K562 and Jurkat cell lines.
IT **256949-67-4P 256949-68-5P 256949-69-6P 256949-70-9P**
RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(prepn., antiproliferative activity, and DNA-binding pyrrolobenzodiazepines contg. oligopyrrole carriers)
RN 256949-67-4 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-(3-amino-3-iminopropyl)-1-methyl-4-[[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

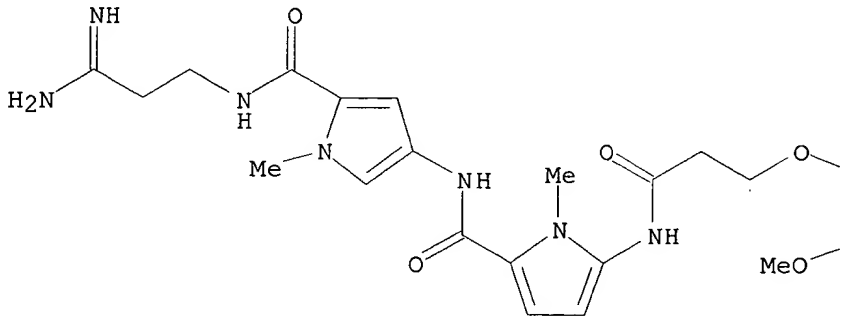


● HCl

RN 256949-68-5 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-(3-amino-3-iminopropyl)-1-methyl-4-[[[1-methyl-5-[[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

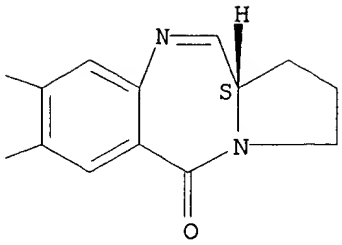
Absolute stereochemistry.

PAGE 1-A



● HCl

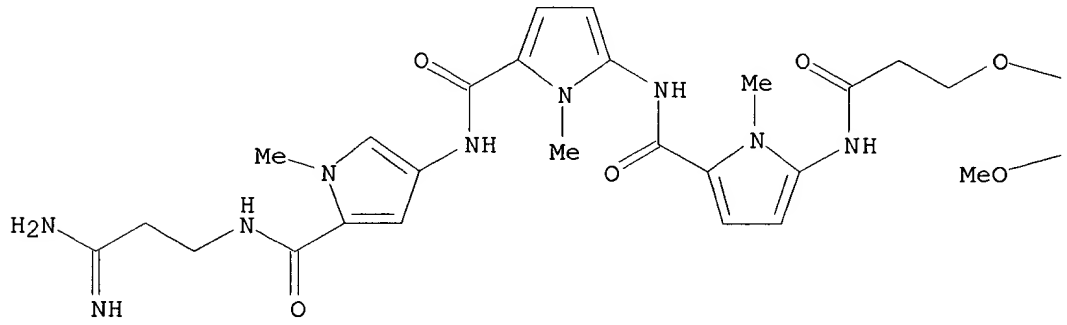
PAGE 1-B



RN 256949-69-6 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-[5-[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl-5-[[[1-methyl-5-[[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

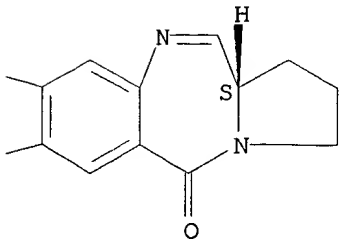
Absolute stereochemistry.

PAGE 1-A



● HCl

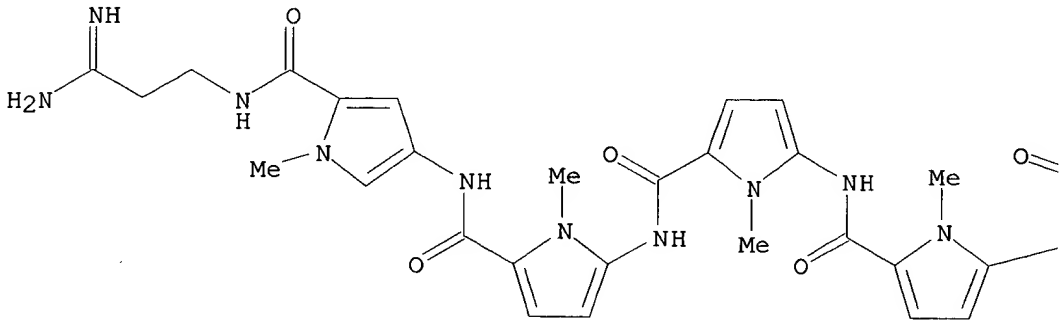
PAGE 1-B



RN 256949-70-9 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-[5-[[[5-[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-methyl-1H-pyrrol-2-yl]-1-methyl-5-[[[1-methyl-5-[[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

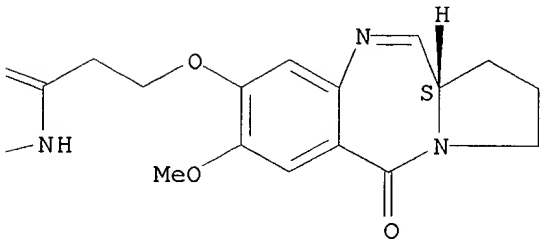
Absolute stereochemistry.

PAGE 1-A



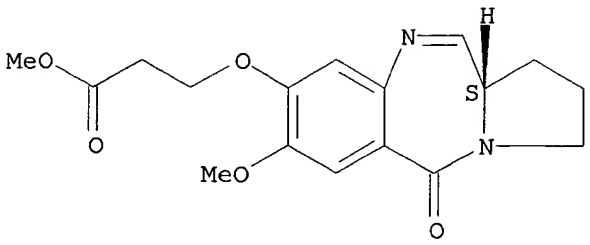
● HCl

PAGE 1-B



IT **219562-69-3P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., antiproliferative activity, and DNA-binding pyrrolobenzodiazepines contg. oligopyrrole carriers)
RN 219562-69-3 CAPLUS
CN Propanoic acid, 3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

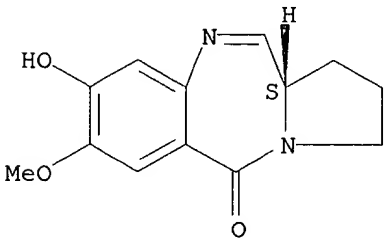
Absolute stereochemistry. Rotation (+).



RE.CNT 39
RE
(1) Arcamone, F; Gazz Chim Ital 1967, V97, P1097 CAPLUS
(2) Arcamone, F; Giorn Microbiol 1961, V9, P83 CAPLUS
(4) Baraldi, P; Bioorg Med Chem Lett 1998, V8, P3019 CAPLUS
(5) Baraldi, P; Curr Pharm Des 1998, V4, P249 CAPLUS
(6) Bentley, D; Mol Cell Biol 1986, V6, P3481 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

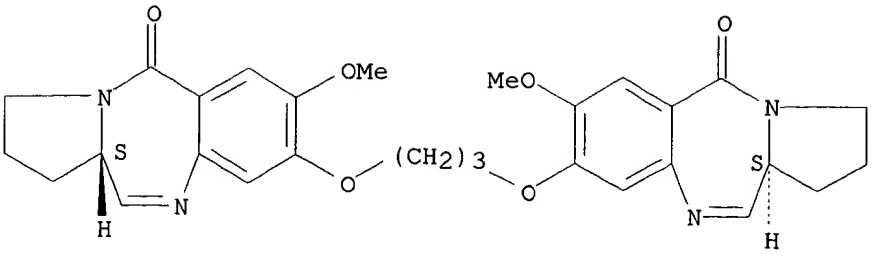
L26 ANSWER 6 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:676295 CAPLUS
DN 132:18480
TI Molecular modeling of a sequence-specific DNA-binding agent based on the pyrrolo[2,1-c][1,4]benzodiazepines
AU Adams, Lesley J.; Jenkins, Terence C.; Banting, Lee; Thurston, David E.
CS CRC Gene Targeted Drug Design Research Group, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, UK
SO Pharm. Pharmacol. Commun. (1999), 5(9), 555-560
CODEN: PPCOFN; ISSN: 1460-8081
PB Royal Pharmaceutical Society of Great Britain
DT Journal
LA English
AB The CHARMm force field was used for the first time to model the tricyclic pyrrolobenzodiazepine (PBD) ring system. This system forms the core of the well known sequence-selective DNA-interactive anthramycin-type antitumor antibiotics. The results agreed with previous results obtained using the AMBER and X-PLOR force fields. The simple family member DC-81 preferentially binds in the 5S orientation with S-stereochem. at the C11 position of the PBD and with the A-ring of the mol. oriented towards the 5' end of the covalently bound strand. The modeling studies and energetic analyses also support the observation that the mols. have a sequence preference for the purine-guanine-purine motif.
IT **81307-24-6**, DC-81 **140676-21-7**, DSB-120
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(mol. modeling of a sequence-specific DNA-binding agent based on the pyrrolo[2,1-c][1,4]benzodiazepines)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 140676-21-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

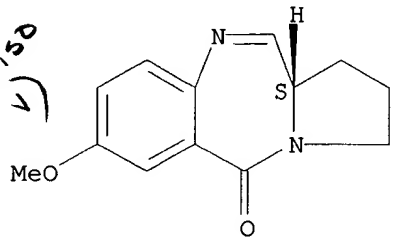
Absolute stereochemistry.



RE.CNT 14
RE
(1) Adams, L; Pharm Sci 1995, V1, P151 CAPLUS
(2) Arora, S; Acta Cryst 1979, VB35, P2945 CAPLUS
(3) Brooks, B; J Comp Chem 1983, V4, P187 CAPLUS
(4) Fletcher, D; J Chem Inf Comp Sci 1996, V36, P746 CAPLUS
(5) Jenkins, T; Eur J Biochem 1993, V213, P1175 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

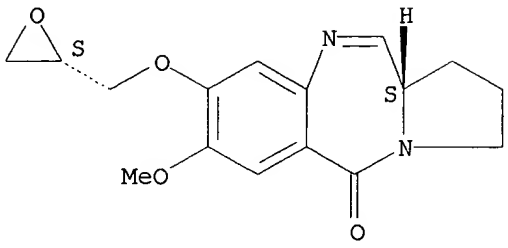
L26 ANSWER 7 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:615557 CAPLUS
DN 132:207668
TI New methods for the synthesis of natural products
AU Melekhov, Alexey G.
CS Iowa State Univ., Ames, IA, USA
SO (1999) 83 pp. Avail.: UMI, Order No. DA9924747
From: Diss. Abstr. Int., B 1999, 60(4), 1613
DT Dissertation
LA English
AB Unavailable
IT **133954-34-4P**, 8-Deoxy-DC-81
RL: SPN (Synthetic preparation); PREP (Preparation)
(new methods for the synthesis of natural products)
RN 133954-34-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



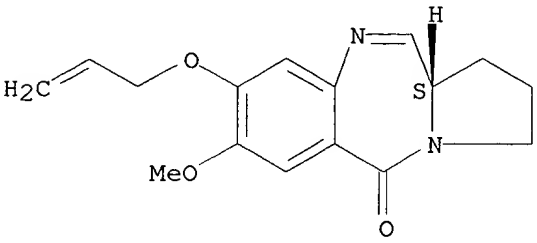
L26 ANSWER 8 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:583940 CAPLUS
DN 132:89603
TI Design, Synthesis, and Evaluation of a Novel Sequence-Selective Epoxide-Containing DNA Cross-Linking Agent Based on the Pyrrolo[2,1-c][1,4]benzodiazepine System
AU Wilson, Stuart C.; Howard, Philip W.; Forrow, Stephen M.; Hartley, John A.; Adams, Lesley J.; Jenkins, Terence C.; Kelland, Lloyd R.; Thurston, David E.
CS CRC Gene Targeted Drug Design Research Group School of Pharmacy and Biomedical Sciences, University of Portsmouth, Hants., PO1 2DT, UK
SO J. Med. Chem. (1999), 42(20), 4028-4041
CODEN: JMCMAR; ISSN: 0022-2623 Oct.
PB American Chemical Society
DT Journal
LA English
OS CASREACT 132:89603
AB Synthetic routes have been investigated to prep. a novel C8-epoxide-functionalized pyrrolo[2,1-c][1,4]benzodiazepine 1 as a potential sequence-selective DNA crosslinking agent (Wilson et al. Tetrahedron Lett. 1995, 36, 6333-6336). A successful synthesis was accomplished via a 10-step route involving a pro-N10-Fmoc cleavage method that should have general applicability to other pyrrolobenzodiazepine (PBD) mols. contg. acid- or nucleophile-sensitive groups. During the course of this work, a one-pot reductive cyclization procedure for the synthesis of PBD N10-C11 imines from nitro di-Me acetals was also discovered, although this method results in C11a racemization which can reduce DNA binding affinity and cytotoxicity. The target epoxide 1 was shown by thermal denaturation studies to have a significantly higher DNA-binding affinity than the parent DC-81 or the C8-propenoxy-PBD, which is structurally similar but lacks the epoxide moiety. The time course of effects upon thermal denaturation indicated a rapid initial binding phase followed by a slower phase consistent with the stepwise crosslinking of DNA obsd. for a difunctional agent. This was confirmed by an electrophoretic assay which demonstrated efficient induction of interstrand cross-links in plasmid DNA at concns. >1 .mu.M. Higher levels of interstrand crosslinking were obsd. at 24 h compared to 6 h incubation. A Taq polymerase stop assay indicated a preference for binding to guanine-rich sequences as predicted for bis-alkylation in the minor groove of DNA by epoxide and imine moieties. The pattern of stop sites could be partly rationalized by mol. modeling studies which suggested low-energy models to account for the obsd. binding behavior. The epoxide PBD 1 was shown to have significant cytotoxicity (45-60 nM) in the A2780, CH1, and CH1cisR human ovarian carcinoma cell lines and an IC50 of 0.2 .mu.M in A2780cisR. The significant activity of 1 in the cisplatin-resistant CH1cisR cell line (IC50 = 47 nM) gave a resistance factor of 0.8 compared to the parent cell line, demonstrating no cross-resistance with the major groove crosslinking agent cisplatin.
IT **171002-52-1P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design, synthesis, and evaluation of novel sequence-selective epoxide-contg. DNA crosslinking agent based on pyrrolo[2,1-c][1,4]benzodiazepine system)
RN 171002-52-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-[(2S)-oxiranylmethoxy]-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



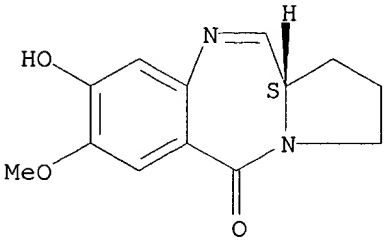
IT **251109-31-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(intermediate; prepn., thermal stability with CT-DNA, and in vitro cytotoxicity)
RN 251109-31-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(2-propenyloxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **81307-24-6**, DC 81 **140676-21-7**, DSB 120
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thermal stability with CT-DNA and in vitro cytotoxicity)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

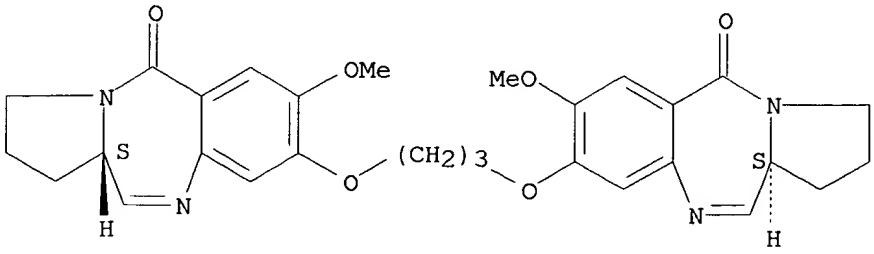
Absolute stereochemistry.



RN 140676-21-7 CAPLUS

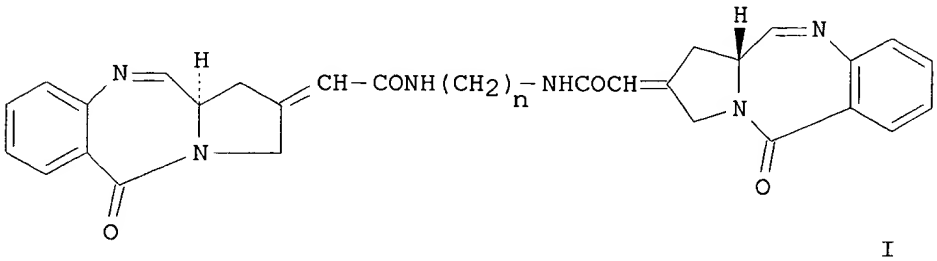
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 59
RE
(1) Adams, L; Pharm Sci 1995, V1, P151 CAPLUS
(2) Armstrong, R; J Am Chem Soc 1992, V114, P3144 CAPLUS
(3) Arora, S; Acta Crystallogr 1979, VB35, P2945 CAPLUS
(5) Bose, D; J Am Chem Soc 1992, V114, P4939 CAPLUS
(8) Brooks, B; J Comput Chem 1983, V4, P187 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 9 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:444659 CAPLUS
DN 131:199684
TI Design and efficient synthesis of novel DNA interstrand crosslinking agents. C(2)-linked pyrrolo[2,1-c][1,4]benzodiazepine dimers
AU Reddy, B. S. Praveen; Damayanthi, Yalamati; Lown, J. William
CS Department Chemistry, Univ. Alberta, Edmonton, AB, T6G 2G2, Can.
SO Synlett (1999), (7), 1112-1114
CODEN: SYNLES; ISSN: 0936-5214
PB Georg Thieme Verlag
DT Journal
LA English
OS CASREACT 131:199684
GI



I

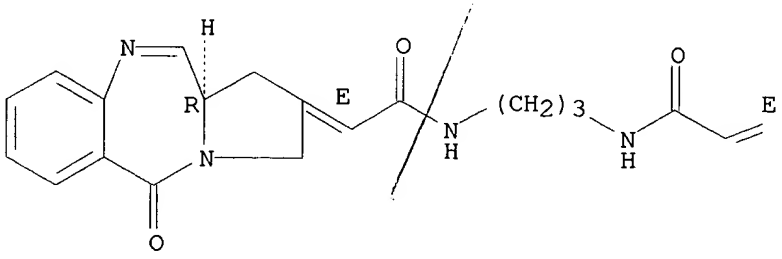
AB The design and facile synthesis of C(2)-linked pyrrolo[2,1-c][1,4]benzodiazepines I (n = 3-5) are described. The compds. are prepd. with varying degrees of linker length to probe the structural requirements for optimal DNA interstrand crosslinking. The products formed are exclusively of the E-configuration.

IT **241489-22-5P 241489-23-6P 241489-24-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of amide-linked pyrrolobenzodiazepine dimers)

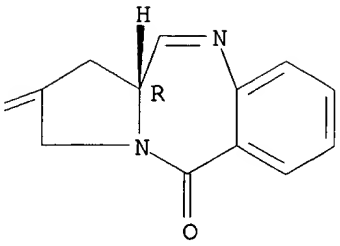
RN 241489-22-5 CAPLUS
CN Acetamide, N,N'-1,3-propanediylbis[2-[(11aR)-5,11a-dihydro-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene]-, (2E,2'E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



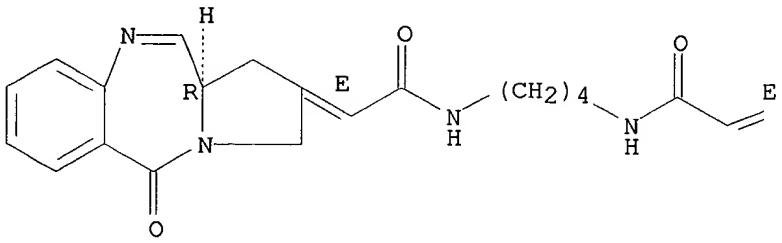
PAGE 1-B



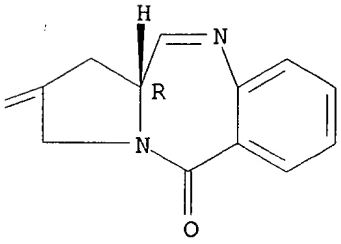
RN 241489-23-6 CAPLUS
CN Acetamide, N,N'-1,4-butanediylbis[2-[(11aR)-5,11a-dihydro-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene]-, (2E,2'E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



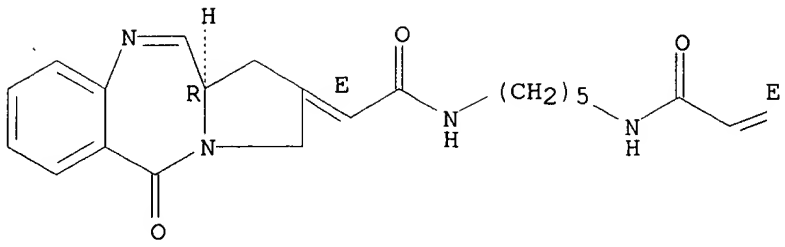
PAGE 1-B



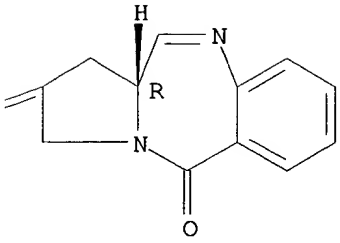
RN 241489-24-7 CAPLUS
CN Acetamide, N,N'-1,5-pentanediylbis[2-[(11aR)-5,11a-dihydro-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene]-, (2E,2'E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

PAGE 1-A



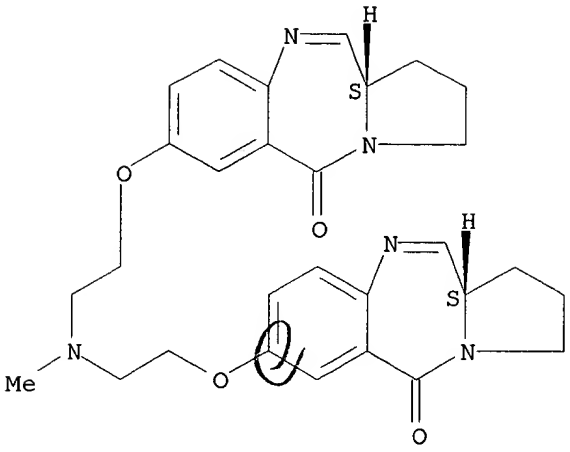
PAGE 1-B



RE.CNT 13
RE
(1) Bose, D; J Am Chem Soc 1992, V114, P4939 CAPLUS
(3) Dervan, P; Science 1986, V232, P464 CAPLUS
(4) Hurley, L; Chem Res Toxicol 1988, V1, P258 CAPLUS
(5) Hurley, L; Trends Pharmacol Res 1988, V9, P402 CAPLUS
(6) Mountzouris, J; J Med Chem 1994, V37, P3132 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 10 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:346781 CAPLUS
DN 131:140917
TI Biological effects of a bifunctional DNA cross-linker. II. Generation of micronuclei and attached micronuclear-like structures
AU Kurek, Kyle; Matsumoto, Lloyd; Gustafson, Gary; Pires, Richard; Tantravahi, Umadevi; Suggs, J. William
CS Division of Biology and Medicine, Brown University, Providence, RI, 02912, USA
SO Mutat. Res. (1999), 426(1), 89-94
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier Science B.V.
DT Journal
LA English
AB Madin-Darby bovine kidney (MDBK) cells were treated with the bifunctional DNA cross-linker, L-7, to examine the generation of micronuclei and other nuclear abnormalities. The preceding paper demonstrates that L-7 treatment induces the formation of triradial and quadriradial chromosomes in MDBK cells. These chromosomes are believed to result from interduplex DNA cross-links formed between G-C rich centromeric satellite DNA regions on non-sister chromatids. Treatment produces a majority of centromere-pos. micronuclei. In addn., many daughter cells remain attached by chromatin bridges which are sometimes beaded with micronuclei. Up to 15% of cell nuclei become lobular and fused with numerous micronuclear-like structures attached to their membranes. These attached structures are classified as attached micronuclear-like structures (AMNLS). Fluorescence in situ hybridization (FISH) using a centromeric satellite sequence was performed on treated cells. Hybridization reveals that intercellular bridges are composed of centromeric sequences and initiate at centromeric foci in daughter cells. Furthermore, the majority of junctions between AMNLS and nuclei contain an enhancement of centromeric signal. The frequency of AMNLS appears dependent on the concn. of L-7 and the duration of treatment. Similar results were found for the generation of cross-linked chromosome products in the previous paper. We suggest that AMNLS result from the abnormal mitotic segregation of cross-linked chromosome products.
IT **123064-64-2**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(biol. effects of bifunctional DNA cross-linker. II. Generation of micronuclei and attached micronuclear-like structures)
RN 123064-64-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,7'-[(methylimino)bis(2,1-ethanediyloxy)]bis[1,2,3,11a-tetrahydro-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

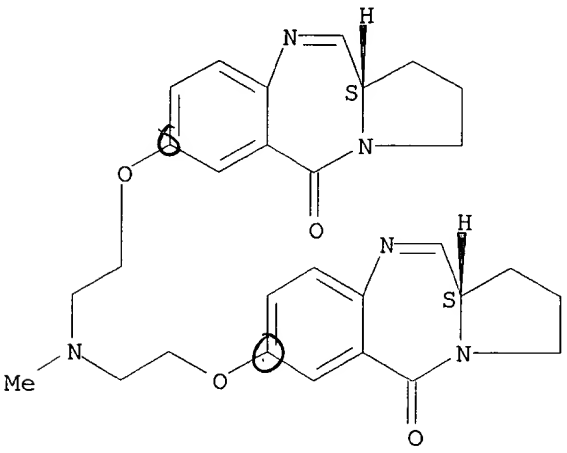
Absolute stereochemistry.



RE.CNT 29
RE
(2) Brinkley, B; Aneuploidy: Etiology and Mechanisms 1985, V36, P243 CAPLUS
(4) Charron, M; Chromosoma 1991, V100, P97 CAPLUS
(5) Davidson, S; Eur J Cancer 1992, V28, P362 CAPLUS
(6) Eastmond, D; Environ Mol Mutagen 1989, V13, P34 CAPLUS
(7) Farmer, J; Nucleic Acids Res 1991, V19, P899 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 11 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:346774 CAPLUS
DN 131:111396
TI Biological effects of a bifunctional DNA crosslinker. I. Generation of triradial and quadriradial chromosomes
AU Matsumoto, L.; Kurek, K.; Larocque, K.; Gustafson, G.; Pires, R.; Zhang, J.; Tantravahi, U.; Suggs, J. W.
CS Departnent of Biology, Rhode Island College, Providence, RI, 02908-1991, USA
SO Mutat. Res. (1999), 426(1), 79-87
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier Science B.V.
DT Journal
LA English
AB Interduplex crosslinks by a bifunctional anthramycin DNA crosslinker produced triradial and quadriradial chromosomes. The crosslinker alkylates guanine at N-2. Bovine chromosomes contain GC-rich d. satellite DNAs at the centromeric heterochromatin and is the basis for the formation of triradial and quadriradial chromosomes at the centromeres. The in situ crosslinking of interphase chromosomes indicates that the distance between centromeres is 17.5 .ANG.. We conclude that the nuclear matrix assocd. DNA in the centromeric heterochromatin of interphase chromosomes are positioned close enough for crosslinking to occur. We propose a model for the generation of triradial and quadriradial chromosomes based upon the no. of interduplex crosslinks between two chromosomes.
IT **123064-64-2**
RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(triradial and quadriradial chromosomes generated by the DNA-crosslinking agent L-7)
RN 123064-64-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,7'-[(methylimino)bis(2,1-ethanediyloxy)]bis[1,2,3,11a-tetrahydro-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

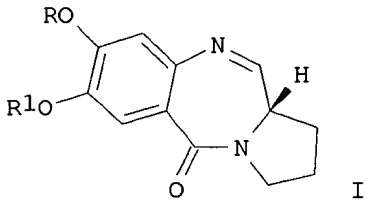
Absolute stereochemistry.



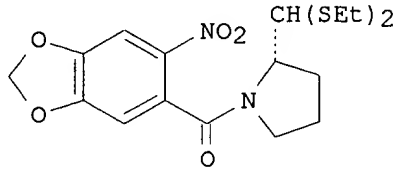
RE.CNT 30
RE
(1) Bodell, W; Mutat Res 1990, V233, P203 CAPLUS

(3) Brooks, B; Comput Chem 1983, V4, P187 CAPLUS
(5) Charron, M; Chromosoma 1991, V100, P97 CAPLUS
(8) Farmer, J; Nucleic Acids Res 1991, V19, P899 CAPLUS
(10) Fujiwara, Y; Br J Cancer 1993, V67, P1285 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 12 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:304467 CAPLUS
DN 131:18989
TI Effect of A-ring modifications on the DNA-binding behavior and cytotoxicity of pyrrolo[2,1-c][1,4]benzodiazepines
AU Thurston, David E.; Bose, D. Subhas; Howard, Philip W.; Jenkins, Terence C.; Leoni, Alberto; Baraldi, Pier G.; Guiotto, Andrea; Cacciari, Barbara; Kelland, Lloyd R.; Foloppe, Marie-Paule; Rault, Sylvain
CS CRC Gene Targeted Drug Design Research Group School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth Hants, P01 2DT, UK
SO J. Med. Chem. (1999), 42(11), June 3, 1951-1964
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



I



II

AB Several A-ring-modified analogs of the DNA-binding antitumor agent DC-81 I (R = H, R1 = Me) have been synthesized in order to study structure-reactivity/cytotoxicity relationships. For two mols., the modifications required the addn. of a fourth ring to give the novel dioxolo[4,5-h]- and dioxano[5,6-h]pyrrolo[2,1-c][1,4]benzodiazepin-11-one (PBD) ring systems, resp. Another three analogs have the native benzenoid A-ring replaced with pyridine, diazine, or pyrimidine rings to give the novel pyrrolo[2,1-c][1,4]pyridodiazepine, pyrrolo[2,1-c][1,4]diazinodiazepine, and pyrrolo[2,1-c][1,4]pyrimidinodiazepine systems, resp. The other new analogs have extended chains at the C8-position of the DC-81 structure. During the synthesis of these compds., a novel tin-mediated regiospecific cleavage reaction of the dioxole intermediate II was discovered, leading to the previously unknown iso-DC-81 I (R = Me, R1 = H). In addn., an unusual simultaneous nitration-oxidn. reaction of 4-(3-hydroxypropoxy)-3-methoxybenzoic acid was found to produce 3-(4-carboxy-2-methoxy-5-nitrophenoxy)propanoic acid, a key intermediate, in high yield. In general, the results of cytotoxicity and DNA-binding studies indicated that none of the changes made to the A-ring of the PBD system significantly improved either binding affinity or cytotoxicity in comparison to DC-81. This result suggests that the superior potency of natural products such as anthramycin, tomaymycin, and sibiromycin is due entirely to differences in C-ring structure, and in particular exo or endo unsatn. at the C2-position and C2-substituents contg. unsatn. This study also provided information regarding the influence of A-ring substitution pattern on the relative stability of the interconvertible N10-C11 carbinolamine, carbinolamine Me ether, and imine forms of PBDs.

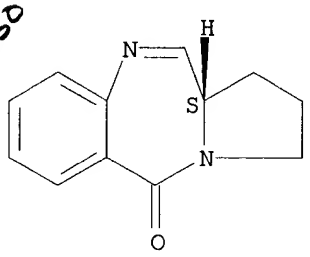
IT **72435-89-3 81307-24-6 81422-30-2**
127810-79-1 226559-61-1
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(prepn., cytotoxicity, and DNA-binding behavior of pyrrolobenzodiazepines)

RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Proviso

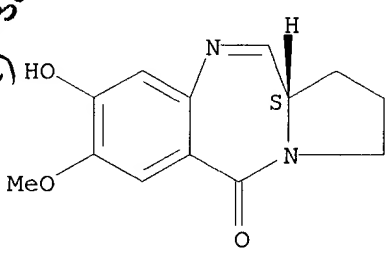
Form III



RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Proviso 2(i)

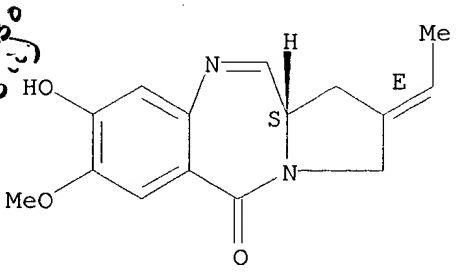


RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

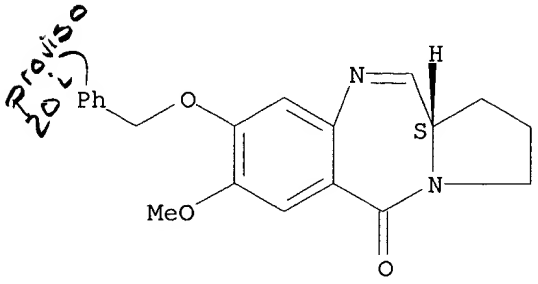
Proviso 13(i)(j)

Form II



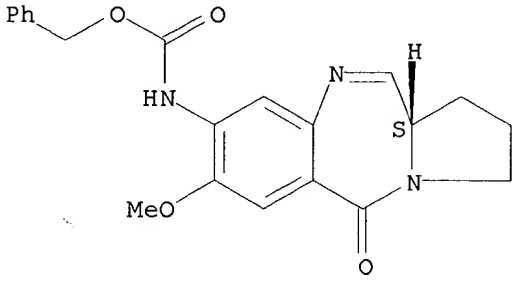
RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



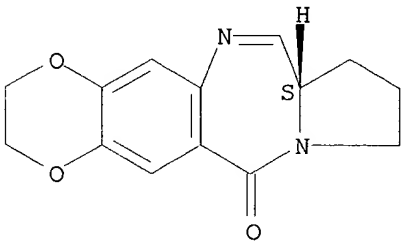
RN 226559-61-1 CAPLUS
CN Carbamic acid, [(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **226559-42-8P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., cytotoxicity, and DNA-binding behavior of pyrrolobenzodiazepines)
RN 226559-42-8 CAPLUS
CN 12H-1,4-Dioxino[2,3-h]pyrrolo[2,1-c][1,4]benzodiazepin-12-one, 2,3,7a,8,9,10-hexahydro-, (7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

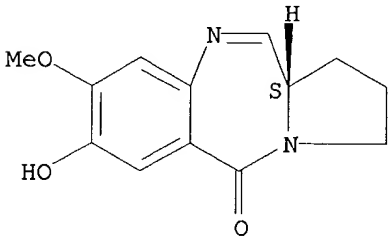


IT **147778-99-2P 219562-69-3P 226559-38-2P**

226559-39-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., cytotoxicity, and DNA-binding behavior of pyrrolobenzodiazepines)

RN 147778-99-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-hydroxy-8-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

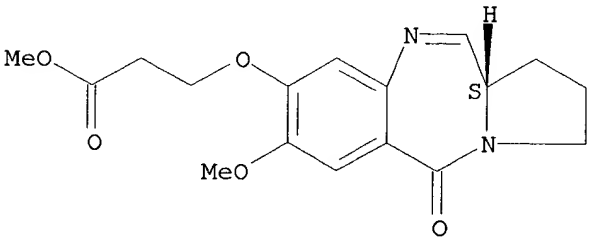
Absolute stereochemistry. Rotation (+).



20

RN 219562-69-3 CAPLUS
CN Propanoic acid, 3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

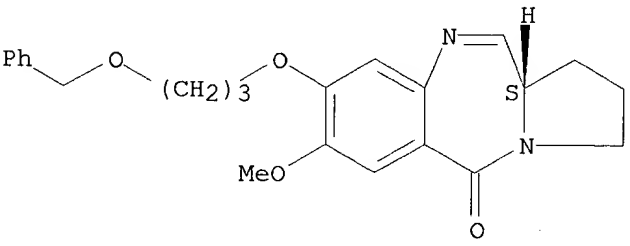
Absolute stereochemistry. Rotation (+).



16a

RN 226559-38-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-[3-(phenylmethoxy)propoxy]-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

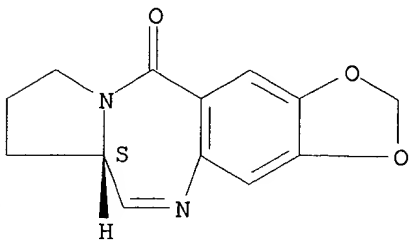


16b

RN 226559-39-3 CAPLUS

CN 11H-1,3-Dioxolo[4,5-h]pyrrolo[2,1-c][1,4]benzodiazepin-11-one, 6a,7,8,9-tetrahydro-, (6aS)- (9CI) (CA INDEX NAME)

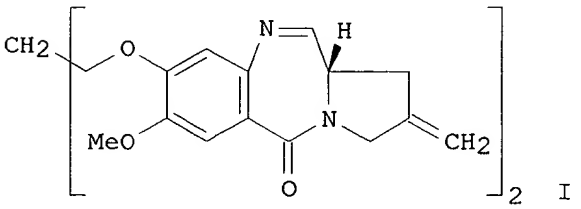
Absolute stereochemistry. Rotation (+).



23

RE.CNT 47
RE
(1) Althuis, T; J Med Chem 1976, V20, P146 CAPLUS
(2) Baraldi, P; J Med Chem 1994, V37, P4329 CAPLUS
(3) Barkley, M; Biochemistry 1986, V25, P3021 CAPLUS
(4) Beckwith, A; J Chem Soc C 1968, P2756 CAPLUS
(5) Bock, L; US 2755273 1956 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 13 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:273645 CAPLUS
DN 131:116218
TI Synthesis of a novel C2/C2'-exo unsaturated pyrrolobenzodiazepine cross-linking agent with remarkable DNA binding affinity and cytotoxicity
AU Gregson, Stephen J.; Howard, Philip W.; Thurston, David E.; Jenkins, Terence C.; Kelland, Lloyd R.
CS School of Pharmacy and Biomedical Sciences, CRC Gene Targeted Drug Design Research Group, University of Portsmouth, Portsmouth, Hants, PO1 2DT, UK
SO Chem. Commun. (Cambridge) (1999), (9), 797-798
CODEN: CHCOFS; ISSN: 1359-7345
PB Royal Society of Chemistry
DT Journal
LA English
GI



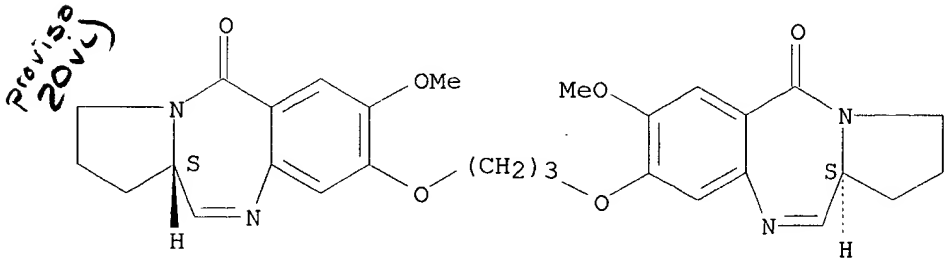
I

AB A C2/C2'-exo unsatd. pyrrolobenzodiazepine dimer (I) has been synthesized which is cytotoxic at the picomolar level and has remarkable covalent DNA binding affinity, raising the melting temp. of duplex-form calf thymus DNA by 34 after 18 h incubation.

IT **140676-21-7**, DSB-120
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. DNA binding and cytotoxicity of pyrrolobenzodiazepine crosslinking agents towards ovarian cancer cells)

RN 140676-21-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



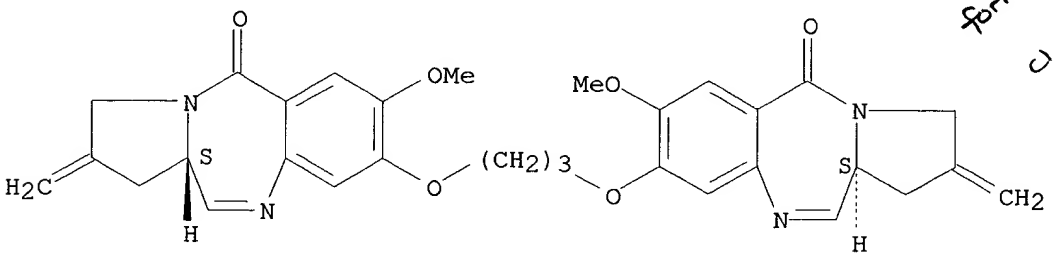
IT **232931-57-6P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(prepn. DNA binding and cytotoxicity of pyrrolobenzodiazepine crosslinking agents towards ovarian cancer cells)

RN 232931-57-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-2-methylene-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



form. II
C1.50

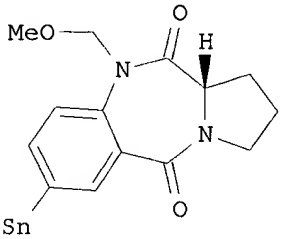
RE.CNT 18

RE

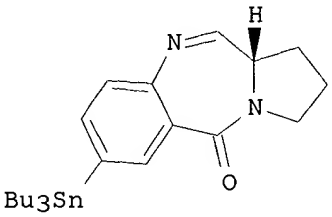
(1) Bose, D; J Am Chem Soc 1992, V114, P4939 CAPLUS
(2) Dangles, O; J Org Chem 1987, V52, P4984 CAPLUS
(3) Deziel, R; Tetrahedron Lett 1987, V28, P4371 CAPLUS
(4) Fukuyama, T; Tetrahedron Lett 1993, V34, P2577 CAPLUS
(5) Jenkins, T; J Med Chem 1994, V37, P4529 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

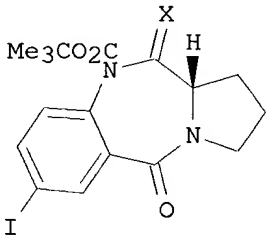
L26 ANSWER 14 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:198610 CAPLUS
DN 131:5244
TI Hydride reductions of 1H-pyrrolo[2,1-c][1,4]-benzodiazepine-5,11-diones: selective reduction of secondary amides to carbinolamines
AU Katsifis, Andrew G.; McPhee, Meredith E.; Ridley, Damon D.
CS Biomedicine and Health Program, ANSTO, Menai, 2234, Australia
SO Aust. J. Chem. (1998), 51(12), 1121-1130
CODEN: AJCHAS; ISSN: 0004-9425
PB CSIRO Publishing
DT Journal
LA English
GI



I



II



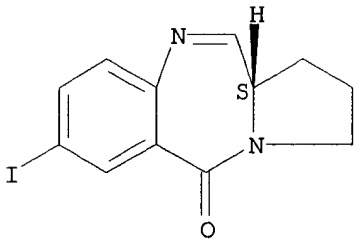
III

AB For the syntheses of radiolabeled pyrrolo[1,4]benzodiazepine antitumor antibiotics a method was required to introduce the unstable carbinolamine functionality prior to the radiolabel. In turn, this required the selective redn. of a secondary amide in the presence of a tertiary amide. Methods that can be used to achieve these outcomes were demonstrated in a series of 1H-pyrrolo[2,1-c][1,4]benzodiazepine-5,11-diones. Thus, LiAlH4 redn. of the (methoxymethyl)pyrrolobenzodiazepinedione I at -60.degree. gave the stannyl imine II in 49% yield, and NaBH4 redn. of the (tert-butoxycarbonyl) dilactam III (X = O) in EtOH at 0.degree. gave III (X = HO, H) in 42% yield.

IT **187083-49-4P 225784-00-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(selective redn. of secondary amide in pyrrolobenzodiazepinediones to carbinolamines)

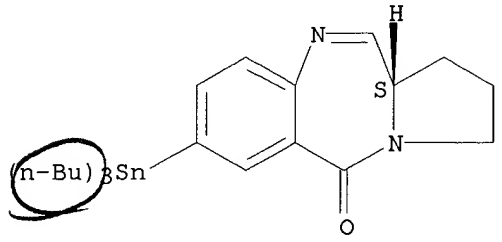
RN 187083-49-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-iodo-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 225784-00-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(tributylstannyl)-, (11aS)- (9CI) (CA INDEX NAME)

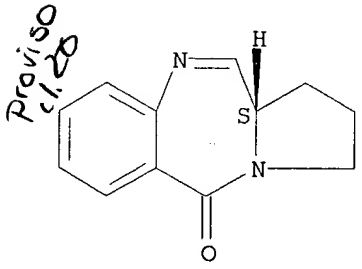
Absolute stereochemistry.



RE.CNT 39
RE
(2) Barkley, M; Biochemistry 1986, V25, P3021 CAPLUS
(3) Behling, J; Tetrahedron Lett 1989, V30, P27 CAPLUS
(4) Farina, V; J Org Chem 1991, V56, P4985 CAPLUS
(5) Flanagan, R; Appl Radiat Isot 1986, V37, P893 CAPLUS
(6) Foster, N; J Radioanal Chem 1981, V65, P95 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

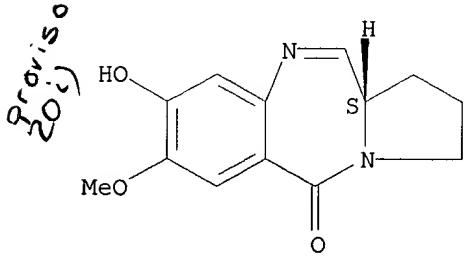
L26 ANSWER 15 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1999:108425 CAPLUS
DN 130:209532
TI A facile and efficient synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antitumor antibiotics: an improved deprotective cyclization method by "clayon"
AU Reddy, B. S. Praveen; Damayanthi, Yalamati; Lown, J. William
CS Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2, Can.
SO Heterocycl. Commun. (1998), 4(6), 497-500
CODEN: HCOMEX; ISSN: 0793-0283
PB Freund Publishing House Ltd.
DT Journal
LA English
OS CASREACT 130:209532
AB A facile procedure for the prepn. of pyrrolo[2,1-c][1,4]benzodiazepine(PBD) imines via ethanethiol deprotective cyclization by using a mild and efficient clay supported ammonium nitrate catalyst is described. A significant improvement in yield over the customary HgCl2/HgO deprotective cyclization method is obsd. and the reaction proceeds with no detectable racemization.
IT **72435-89-3P 81307-24-6P 127810-79-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antitumor antibiotics using clay supported ammonium nitrate catalyst)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



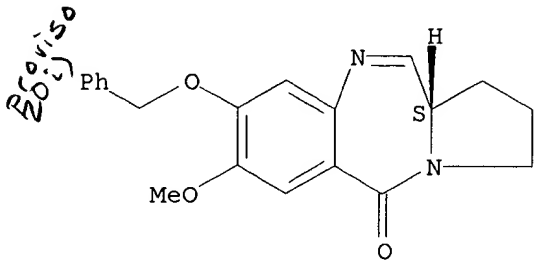
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



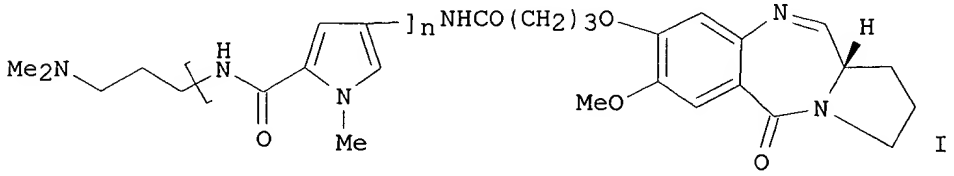
RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 14
RE
(1) Hurley, L; Nature (London) 1979, V282, P529 CAPLUS
(2) Kamal, A; Bioorg Med Chem Lett 1997, V7, P1825 CAPLUS
(3) Kamal, A; Chem Commun 1996, P385 CAPLUS
(4) Kamal, A; Chem Commun 1997, P1015 CAPLUS
(5) Kamal, A; Tetrahedron 1997, V53, P3223 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

D26 ANSWER 16 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1998:777202 CAPLUS
DN 130:125384
TI Design and Synthesis of Novel Pyrrolo[2,1-c][1,4]benzodiazepine-Lexitropsin Conjugates
AU Damayanthi, Yalamati; Reddy, B. S. Praveen; Lown, J. William
CS Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2, Can.
SO J. Org. Chem. (1999), 64(1), 290-292
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 130:125384
GI

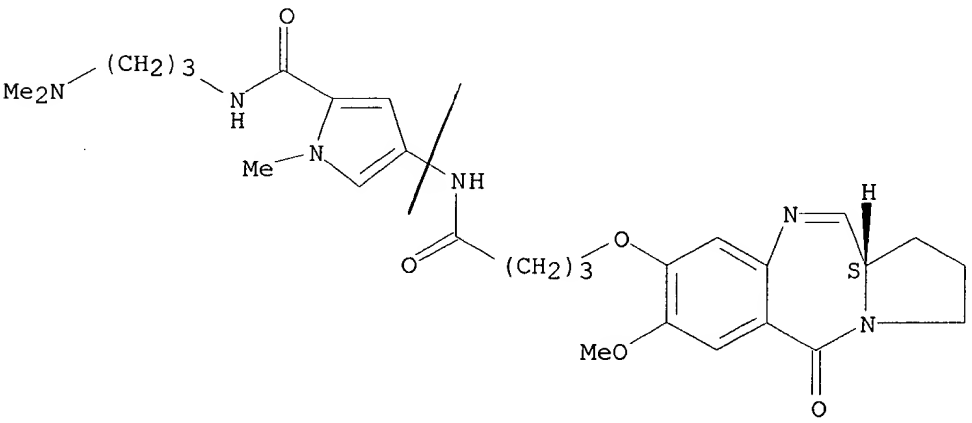


AB A versatile and convenient strategy for the design and synthesis of a series of novel pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-lexitropsin conjugates I (n = 1-3) bonded through the C8 position with a suitable linker of three carbons (overall five-atom spacer) is described. I were designed in order to examine the combined effect of both moieties on DNA sequence selective binding ability and cytotoxicity (no data).

IT **219931-74-5P 219931-75-6P 219931-76-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(design and synthesis of pyrrolobenzodiazepine-lexitropsin conjugates)

RN 219931-74-5 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-[3-(dimethylamino)propyl]-1-methyl-4-[[1-oxo-4-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]butyl]amino]- (9CI) (CA INDEX NAME)

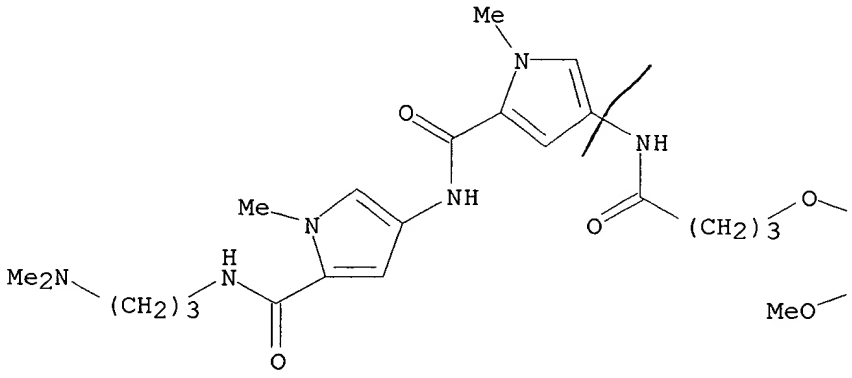
Absolute stereochemistry.



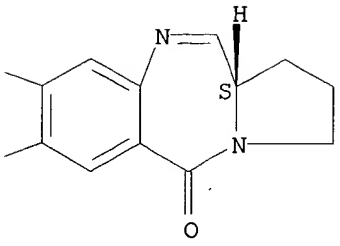
RN 219931-75-6 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-[5-[[[3-(dimethylamino)propyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl-4-[[1-oxo-4-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]butyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



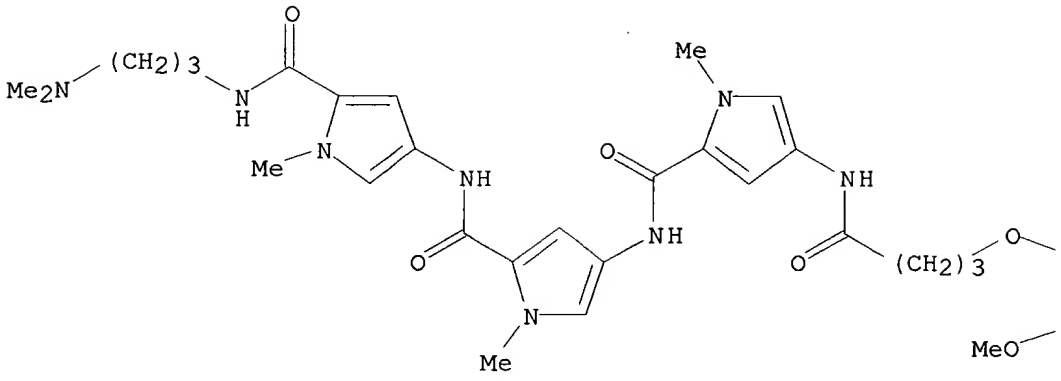
PAGE 1-B



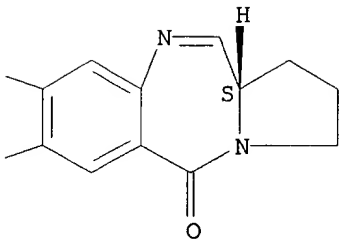
RN 219931-76-7 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-[5-[[[3-(dimethylamino)propyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl-4-[[[1-methyl-4-[[1-oxo-4-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]butyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

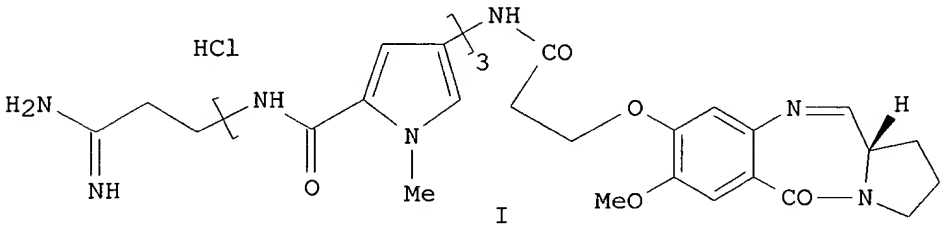


PAGE 1-B

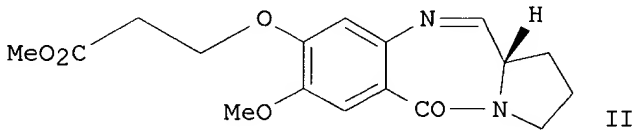


RE.CNT 35
RE
(1) Bose, D; J Am Chem Soc 1992, V114, P4939 CAPLUS
(2) Bose, D; J Chem Soc Chem Commun 1992, P1518 CAPLUS
(3) Cheatham, S; J Med Chem 1988, V31, P583 CAPLUS
(6) Farmer, J; Tetrahedron Lett 1988, V29, P5105 CAPLUS
(7) Fontana, M; Anti-Cancer Drug Design 1992, V7, P131 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 17 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1998:760824 CAPLUS
DN 130:95405
TI Design, synthesis and biological activity of a pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-distamycin hybrid
AU Baraldi, Pier Giovanni; Cacciari, Barbara; Guiotto, Andrea; Leoni, Alberto; Romagnoli, Romeo; Spalluto, Giampiero; Mongelli, Nicola; Howard, Philip W.; Thurston, David E.; Bianchi, Nicoletta; Gambari, Roberto
CS Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SO Bioorg. Med. Chem. Lett. (1998), 8(21), 3019-3024
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 130:95405
GI



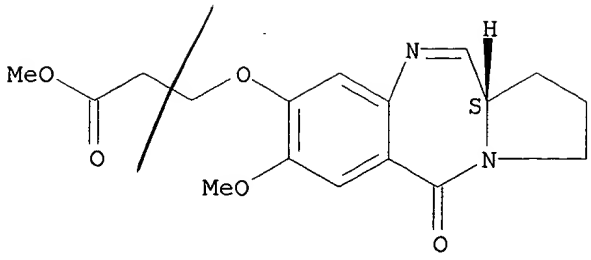
I



II

AB The authors report the synthesis of a new hybrid (I) which is a combination of the naturally occurring antitumor agent distamycin A and the pyrrolo[2,1-c][1,4]benzodiazepine (II), related to naturally occurring anthramycin. The antitumor activity of the hybrid I was tested in vitro and compared to the natural product distamycin A and the PBD II.
IT **219562-69-3P 219562-82-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design, synthesis and biol. activity of a pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-distamycin hybrid)
RN 219562-69-3 CAPLUS
CN Propanoic acid, 3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 219562-82-0 CAPLUS
CN 1H-Pyrrole-2-carboxamide, N-[5-[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl-4-[[[1-methyl-4-[[1-oxo-3-[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

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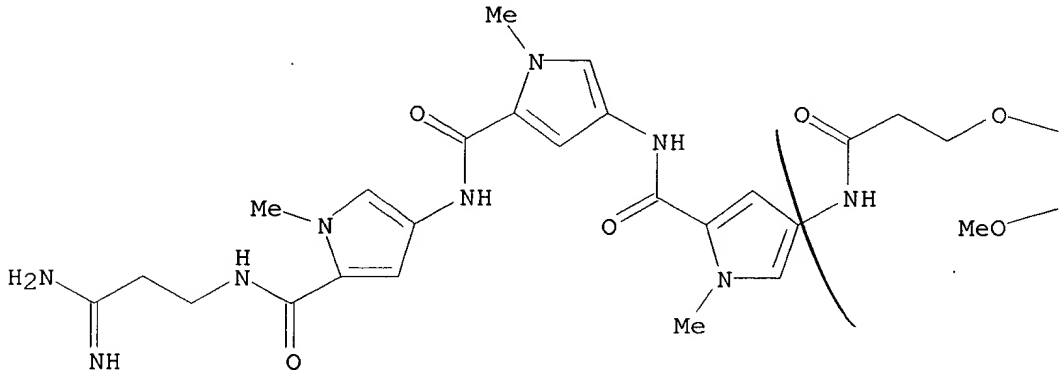
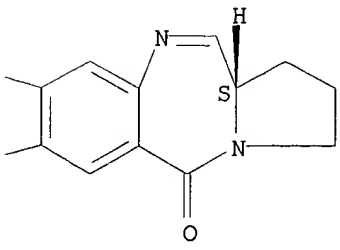


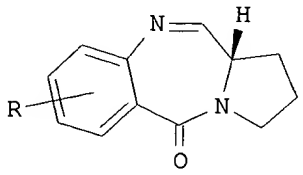
● HCl

PAGE 1-B



RE.CNT 21
RE
(1) Arcamone, F; Gazz Chim Ital 1967, V97, P1097 CAPLUS
(2) Arcamone, F; Gazzetta Chim Ital 1969, V99, P632 CAPLUS
(3) Bianchi, N; Biochem Pharmacol 1996, V52, P1489 CAPLUS
(4) Bianchi, N; J Steroid Biochem Molec Biol 1995, V54, P211 CAPLUS
(5) Del Senno, L; Human Molec Genetics 1992, V1, P354 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 18 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1998:760823 CAPLUS
DN 130:95540
TI Synthesis of novel C7-aryl substituted pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) via pro-N10-Troc protection and Suzuki coupling
AU Guiotto, Andrea; Howard, Philip W.; Baraldi, Pier Giovanni; Thurston, David E.
CS CRC Gene Targeted Drug Design Research Group, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, UK
SO Bioorg. Med. Chem. Lett. (1998), 8(21), 3017-3018
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 130:95540
GI



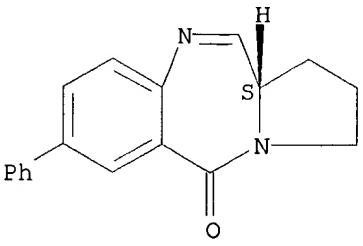
I

AB Novel C7-aryl pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) I (R1 = H, 4'-Me, 3'-NO2, etc.) have been synthesized via Suzuki coupling between a 7-Iodo N10-Troc-protected PBD carbinolamine and com. available boronic acids R'C6H4B(OH)2.

IT **215723-10-7P 219537-15-2P 219537-16-3P**
219537-17-4P 219537-18-5P 219537-19-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and cytotoxicity of aryl pyrrolobenzodiazepines via Suzuki coupling)

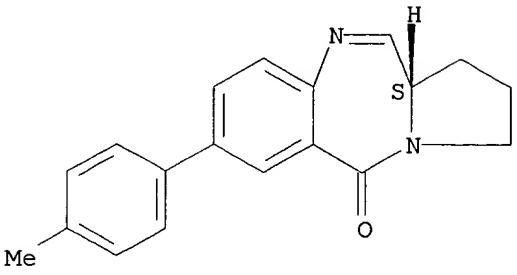
RN 215723-10-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-phenyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



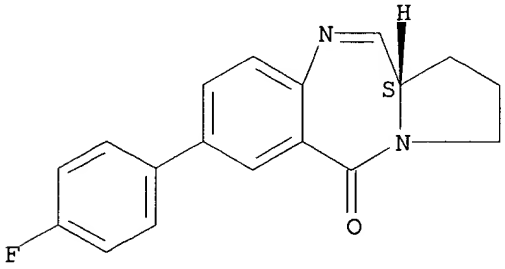
RN 219537-15-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(4-methylphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



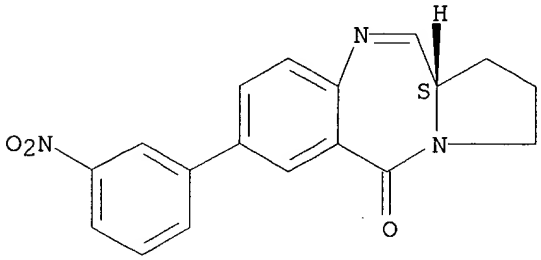
RN 219537-16-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-(4-fluorophenyl)-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



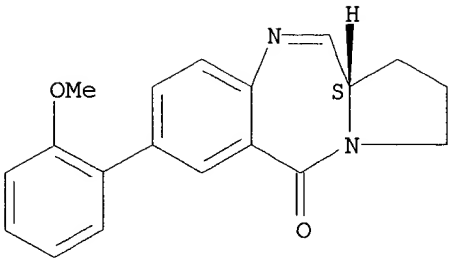
RN 219537-17-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(3-nitrophenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



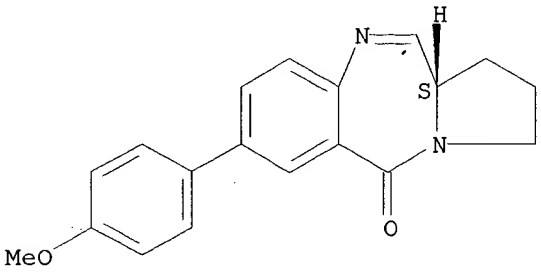
RN 219537-18-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(2-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 219537-19-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(4-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

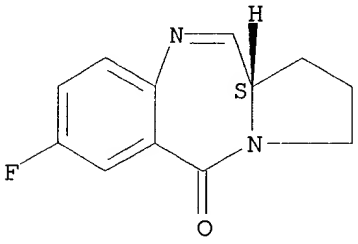
Absolute stereochemistry.



RE.CNT 7
RE
(1) Dong, Q; Tetrahedron Lett 1995, V36, P5681 CAPLUS
(2) Miyaura, N; Chem Rev 1995, V95, P2457 CAPLUS
(3) Puvvada, M; Biochemistry 1997, V36, P2478 CAPLUS
(4) Puvvada, M; Nucleic Acids Res 1993, V21, P3671 CAPLUS
(5) Thurston, D; Chem Rev 1994, V94, P433 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

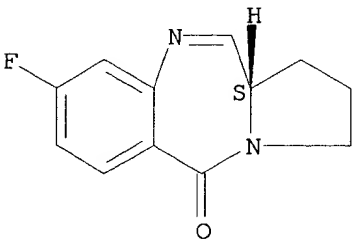
L26 ANSWER 19 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1998:656968 CAPLUS
DN 130:3493
TI DPPE: a convenient replacement for triphenylphosphine in the Staudinger and Mitsunobu reactions
AU O'Neil, Ian A.; Thompson, Stephen; Murray, Clare L.; Kalindjian, S. Barret
CS Dep. Chem., Univ. Liverpool, Liverpool, L69 7ZD, UK
SO Tetrahedron Lett. (1998), 39(42), 7787-7790
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 130:3493
AB DPPE has been shown to replace triphenylphosphine in the Staudinger and Mitsunobu reactions. The resulting bis(phosphine oxide) byproduct is readily removed allowing for rapid and simple purifn. of the reaction mixt.
IT **215723-03-8P 215723-04-9P 215723-05-0P**
215723-06-1P 215723-07-2P 215723-08-3P
215723-09-4P 215723-10-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(use of DPPE in the Staudinger and Mitsunobu reactions)
RN 215723-03-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-fluoro-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 215723-04-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8-fluoro-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

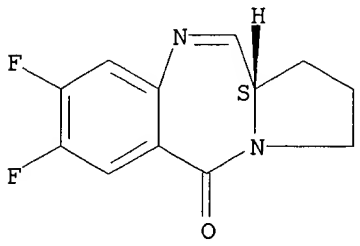
Absolute stereochemistry.



RN 215723-05-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,8-difluoro-1,2,3,11a-

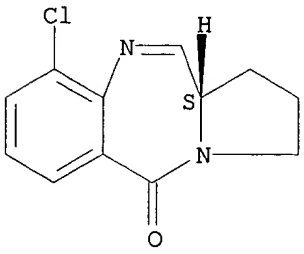
tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



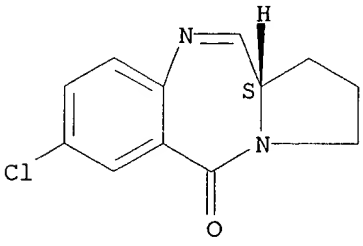
RN 215723-06-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-chloro-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



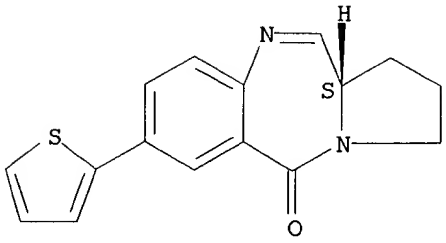
RN 215723-07-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-chloro-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



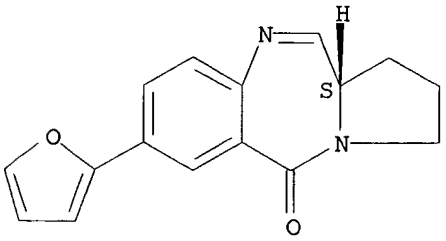
RN 215723-08-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(2-thienyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



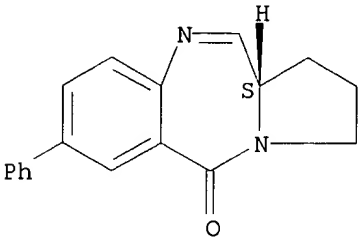
RN 215723-09-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-(2-furanyl)-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



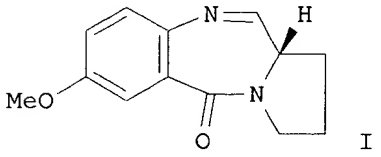
RN 215723-10-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-phenyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 15
RE
(1) Amos, R; J Org Chem 1983, V48, P3598 CAPLUS
(2) Camp, D; Aust J Chem 1988, V41, P1835 CAPLUS
(3) Castro, R; J Org Chem 1996, V61, P7298 CAPLUS
(4) Eguchi, S; J Org Chem 1995, V60, P4006 CAPLUS
(5) Etter, M; J Am Chem Soc 1988, V110, P639 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 20 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1998:617896 CAPLUS
DN 129:302623
TI Synthesis of pyrrolobenzodiazepines via the PIFA oxidation of amines. Synthesis of 8-deoxy DC-81
AU Kraus, George A.; Melekhov, Alex
CS Department of Chemistry, Iowa State University, Ames, IA, 50011, USA
SO Tetrahedron (1998), 54(39), 11749-11754
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science Ltd.
DT Journal
LA English
GI



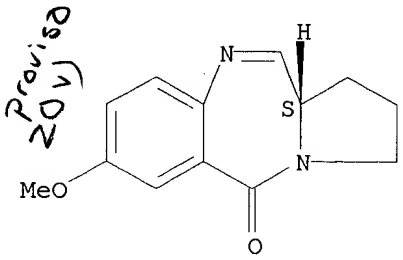
I

AB Bis(trifluoroacetoxy)iodobenzene (PIFA) can be used to introduce the imine moiety into a precursor to the pyrrolobenzodiazepines in 62% yield. This oxidn. completes an efficient four-step synthesis of 8-deoxy DC-81 (I).

IT **133954-34-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(pyrrolobenzodiazepines via PIFA oxidn. of amines)

RN 133954-34-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

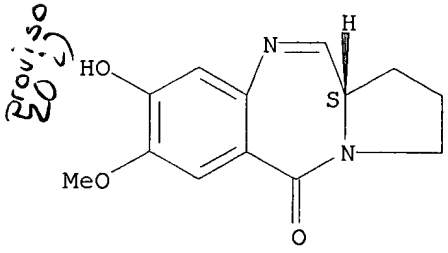
Absolute stereochemistry.



Provisional

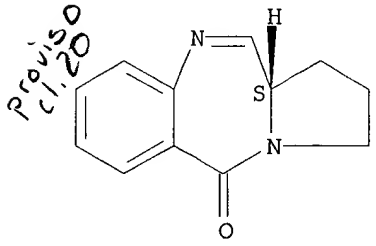
L26 ANSWER 21 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1998:461819 CAPLUS
DN 129:188890
TI A mild and facile reduction of azides to amines by N,N-dimethylhydrazine and catalytic ferric chloride
AU Kamal, Ahmed; Reddy, B. S. Narayan
CS Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad, 500 007, India
SO Chem. Lett. (1998), (7), 593-594
CODEN: CMLTAG; ISSN: 0366-7022
PB Chemical Society of Japan
DT Journal
LA English
OS CASREACT 129:188890
AB Reaction of a variety of azido compds. with N,N-dimethylhydrazine in the presence of a catalytic amt. of ferric chloride hexahydrate in methanol results in excellent yields of the corresponding amino compds. This reductive system is compatible with a wide assortment of functional groups and has also been extended towards the synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics. The redn. and cyclization of (S)-1-(2-azido-4-hydroxy-5-methoxybenzoyl)-2-pyrrolidinecarboxaldehyde gave Antibiotic DC 81 [i.e., (1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-)-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one].
IT **81307-24-6P**, Antibiotic DC 81
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



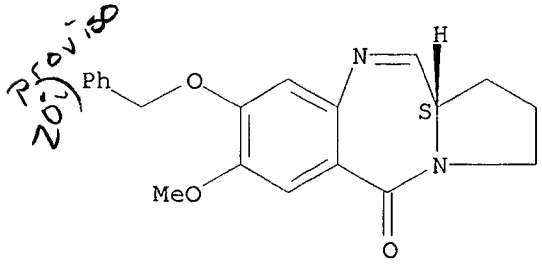
L26 ANSWER 22 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1998:66432 CAPLUS
DN 128:154068
TI A new methodology for the reductive cyclization of .omega.-azido carbonyl compounds mediated by tetrathiomolybdate. Application to an efficient synthesis of pyrrolo[2,1-c][1,4]benzodiazepines
AU Prabhu, Kandikere R.; Sivanand, P. S.; Chandrsekaran, Srinivasan
CS Department Organic Chemistry, Indian Institute Science, Bangalore, 560012, India
SO Synlett (1998), (1), 47-48
CODEN: SYNLES; ISSN: 0936-5214
PB Georg Thieme Verlag
DT Journal
LA English
OS CASREACT 128:154068
AB The .omega.-azido carbonyl compds. on treatment with [PhCH2NEt3]2MoS4 led to the formation of 5-, 6-, and 7-membered cyclic imines in very good yields under mild conditions. This method is applied successfully to an efficient synthesis of 1,4-benzodiazepinones and in particular benzylated DC-81.
IT **72435-89-3P 127810-79-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of pyrrolobenzodiazepines by thiomolybdate-mediated reductive cyclization of .omega.-azido carbonyl compds.)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

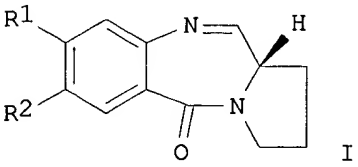


RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L26 ANSWER 23 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1997:538783 CAPLUS
DN 127:220632
TI An efficient synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via reductive cyclization
AU Kamal, Ahmed; Reddy, B. S. Nararyan; Reddy, B. S. Praveen
CS Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad, 500 007, India
SO Bioorg. Med. Chem. Lett. (1997), 7(14), 1825-1828
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
OS CASREACT 127:220632
GI



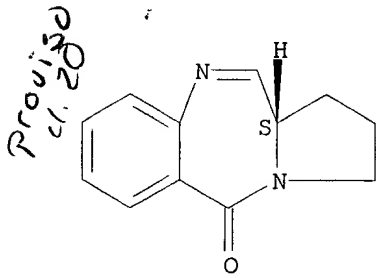
I

AB A new and convenient one-pot synthesis of pyrrolo[2,1-c][1,4]benzodiazepines (PBD) (I; R1 = R2 = H; R1 = OCH2Ph, R2 = OMe; R1 = OH, R2 = OMe) has been achieved by a reductive cyclization employing N,N-dimethylhydrazine and FeCl3.6H2O in good yields.

IT **72435-89-3P 81307-24-6P 127810-79-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of pyrrolobenzodiazepines by reductive cyclization)

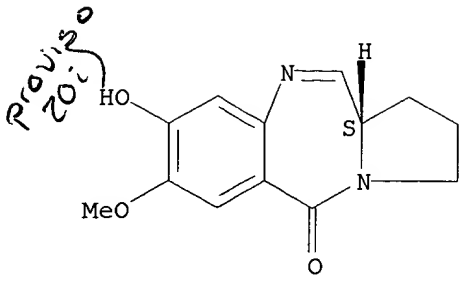
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



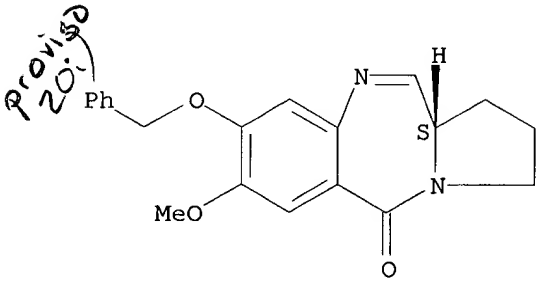
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

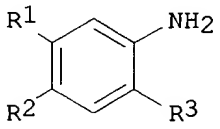


RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

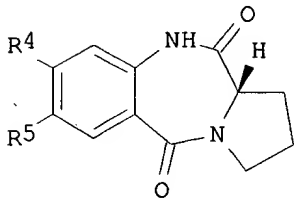
Absolute stereochemistry. Rotation (+).



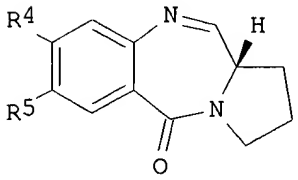
L26 ANSWER 24 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1997:403325 CAPLUS
DN 127:81265
TI Novel biocatalytic reduction of aryl azides: chemoenzymic synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics
AU Kamal, Ahmed; Damayanthi, Y.; Reddy, B. S. Narayan; Lakminarayana, B.; Reddy, B. S. Praveen
CS Indian Inst. Chem. Technol., Hyderabad, 500 007, India
SO Chem. Commun. (Cambridge) (1997), (11), 1015-1016
CODEN: CHCOFS; ISSN: 1359-7345
PB Royal Society of Chemistry
DT Journal
LA English
OS CASREACT 127:81265
GI



I



II



III

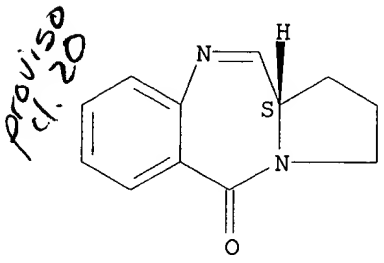
AB The chemoselective redn. of aryl azides to aryl amines (I) (R1 = H,Me; R2 = H, Cl, F, OMe; R3 = H, CO2H, OH), and the synthesis of the imine-contg. pyrrolo[2,1-c][1,4]benzodiazepine DNA-binding antitumor antibiotics (II) and (III) (R4 = H, OH, OCH2Ph; R5 = Me, OMe) by selective biocatalytic reductive cyclization of azido aldehydes, has been achieved by employing baker's yeast.

IT **72435-89-3P 81307-24-6P 127810-79-1P 182508-34-5P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(chemoenzymic synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via biocatalytic redn. of aryl azides)

RN 72435-89-3 CAPLUS

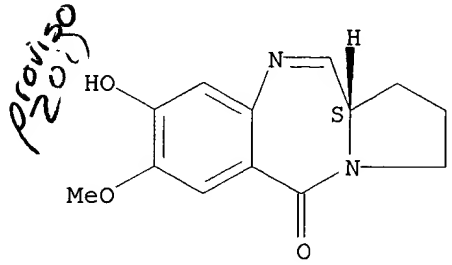
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



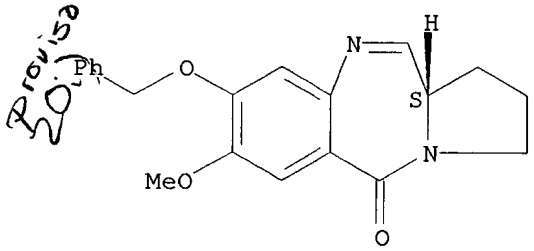
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



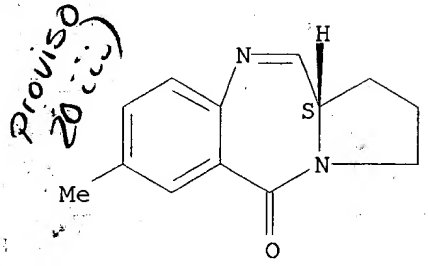
RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



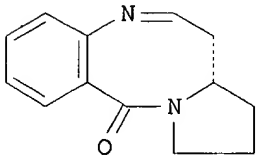
RN 182508-34-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

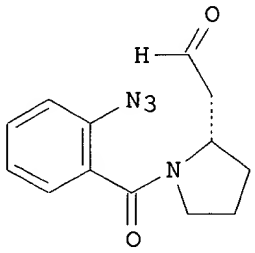


Proviso 20 (c)

L26 ANSWER 25 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1997:349351 CAPLUS
DN 127:81431
TI The synthesis of a novel benzodiazocine via an intramolecular Staudinger/aza-Wittig cyclization
AU O'neil, Ian A.; Murray, Clare L.; Potter, Andrew J.; Kalindjian, S. Barret
CS Department of Chemistry, University of Liverpool, Liverpool, L69 3BX, UK
SO Tetrahedron Lett. (1997), 38(20), 3609-3610
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 127:81431
GI



I

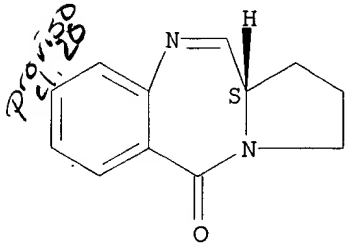


II

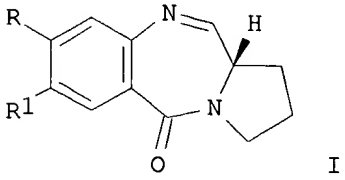
AB The novel pyrrolobenzodiazocine I has been prepd. by an intramol. Staudinger/aza Wittig protocol from the precursor azido aldehyde II in a remarkable 93% yield. Aldehyde II was prepd. by coupling protected homoprolinol with 2-azidobenzoic acid followed by deprotection and oxidn.

IT **72435-89-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of benzodiazocine via Staudinger-aza-Wittig cyclization)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L26 ANSWER 26 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1997:165424 CAPLUS
DN 126:225131
TI Synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics: oxidation of cyclic secondary amine with TPAP
AU Kamal, Ahmed; Howard, Philip W.; Reddy, B. S. Narayan; Reddy, B. S. Praveen; Thurston, David E.
CS Div. Org. Chem., Indian Inst. Chem. Technol., Hyderabad, 500 007, India
SO Tetrahedron (1997), 53(9), 3223-3230
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier
DT Journal
LA English
OS CASREACT 126:225131
GI



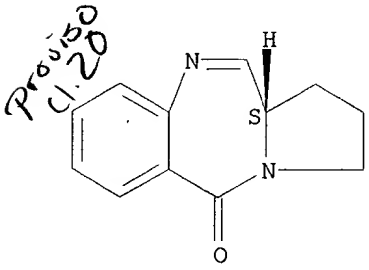
I

AB A facile procedure for the prepn. of the imine form of the pyrrolo[2,1-c][1,4]-benzodiazepine ring system I (R, R1 = H; R = OH, R1 = MeO) by the oxidn. of cyclic secondary amine with catalytic amts. of tetra-n-propylammonium perruthenate (TPAP) and N-methylmorpholine N-oxide (NMO) as a co-oxidant is described. This oxidative method is devoid of side-products and is thus a significant improvement over the Swern oxidn. previously reported.

IT **72435-89-3P 81307-24-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via oxidn. of cyclic secondary amine with tetra-n-propylammonium perruthenate)

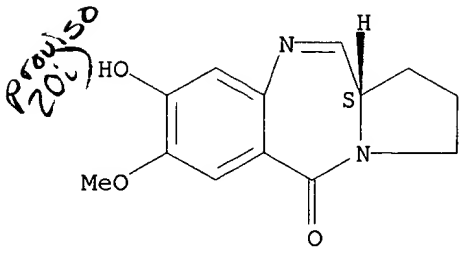
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



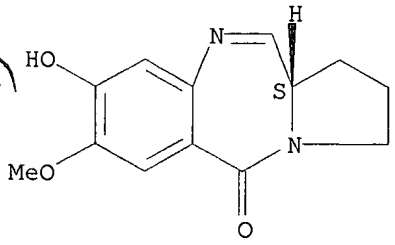
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 27 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1997:164900 CAPLUS
DN 126:139567
TI Inhibition of Bacteriophage T7 RNA Polymerase in Vitro Transcription by DNA-Binding Pyrrolo[2,1-c][1,4]benzodiazepines
AU Puvvada, Madhu S.; Forrow, Stephen A.; Hartley, John A.; Stephenson, Pauline; Gibson, Ian; Jenkins, Terence C.; Thurston, David E.
CS Gene Targeted Drug Design Research Group School of Pharmacy and Biomedical Science, University of Portsmouth, Portsmouth, PO1 2DT, UK
SO Biochemistry (1997), 36(9), 2478-2484
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB The interactions of several pyrrolo[2,1-c][1,4]benzodiazepine (PBD) antitumor antibiotics with linearized plasmid p-GEM-2-N-ras DNA have been analyzed by quant. in vitro transcription (QIVT) and in vitro transcription footprinting (IVTF) methods. A concn.-dependent inhibitory effect of the PBDs on transcription is obsd. using both techniques. The rank order for overall inhibition of transcription by the QIVT method is : sibiromycin > tomaymycin > anthramycin > DC-81 > neothramycin, whereas the IVTF expts. show a different ranking: sibiromycin > anthramycin > neothramycin > tomaymycin. In addn., stimulation of transcription was obsd. at low PBD concns. in both the QIVT and IVTF expts. These results demonstrate unequivocally that the formation of PBD-DNA adducts at AGA-5' base sequences on the transcribed strand results in transcription blockage for all PBDs examd. Furthermore, the sequence of flanking base pairs appears to influence the degree of blocking, with the sequences ACAGAAA-5', AAAGATG-5', AGAGATA-5', and CAAGAAC-5' providing the most pronounced blocks for all PBDs in this system. Neothramycin and tomaymycin cause addnl. blocks at some GGA-5' and TGA-5' sequences. Parallel MPE-Fe(II) footprinting studies have revealed PBD binding sites on both the transcribing and nontranscribing strands, although all transcription blocks detd. from the IVTF assays are due to drug bound on the transcribing DNA template strand.
IT **81307-24-6**, DC-81
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibition of bacteriophage T7 RNA polymerase in vitro transcription by DNA-binding pyrrolo[c][1,4]benzodiazepines)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

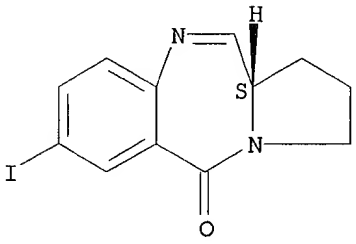
Absolute stereochemistry.



previso 20.)

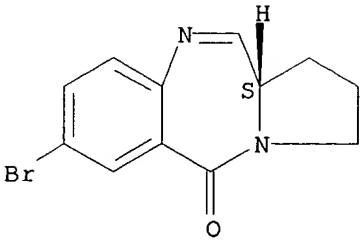
L26 ANSWER 28 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1997:110812 CAPLUS
DN 126:171573
TI The synthesis of functionalized pyrrolo[2,1-c][1,4]benzodiazepines
AU O'Neil, Ian; Murray, Clare L.; Hunter, Rachel C.; Kalindjian, S. Barret; Jenkins, Terry C.
CS Dep. Chem., Univ. Liverpool, Liverpool, L69 3BX, UK
SO Synlett (1997), (1), 75-78
CODEN: SYNLES; ISSN: 0936-5214
PB Thieme
DT Journal
LA English
OS CASREACT 126:171573
AB Two concise and high yielding routes to the pyrrolo[2,1-c][1,4]benzodiazepine ring system are described. Thus, condensation of prolinol with 2-azidobenzoyl chloride gives the corresponding amide. Oxidn. to the aldehyde followed by generation of the phosphoroimine by Staudinger reaction results in ring closure via an aza-Wittig reaction to yield the desired ring system. Alternatively, coupling of prolinol with the appropriate isatoic anhydride yields the corresponding amino alc. Oxidn. with Dess-Martin periodinane yields the title compds. in moderate to good yield. The cytotoxicity of bromo, chloro, and iodo derivs. against human ovarian carcinoma cells was detd. The most active compd. showed IC50 ratios of 0.54 and 1.65.
IT **187083-49-4P 187083-50-7P 187337-77-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of pyrrolobenzodiazepines)
RN 187083-49-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-iodo-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



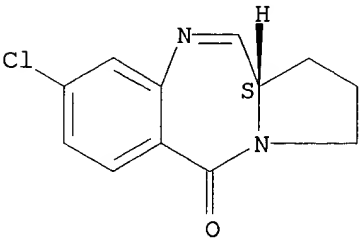
RN 187083-50-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-bromo-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



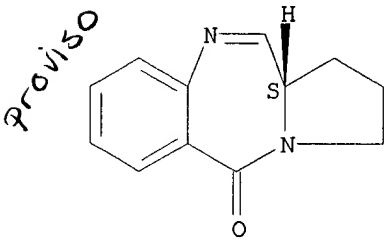
RN 187337-77-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8-chloro-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **72435-89-3P 187083-51-8P 187083-52-9P 187083-53-0P 187083-54-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and antitumor activity of pyrrolobenzodiazepines)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

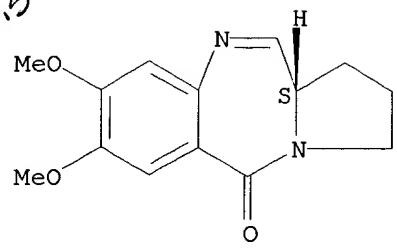
Absolute stereochemistry. Rotation (+).



RN 187083-51-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

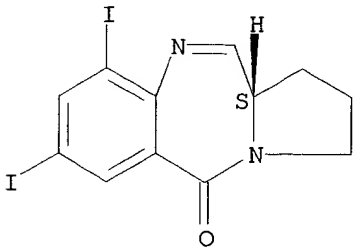
Absolute stereochemistry.

Proviso



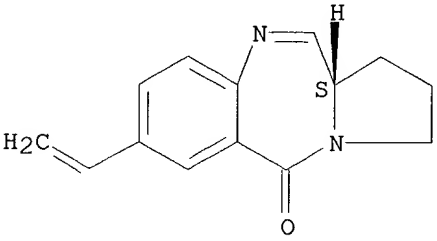
RN 187083-52-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,9-diiodo-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



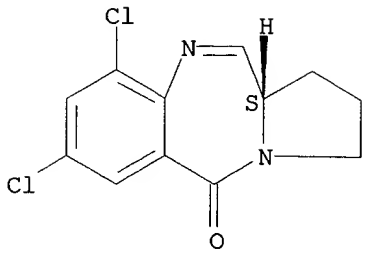
RN 187083-53-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-ethenyl-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



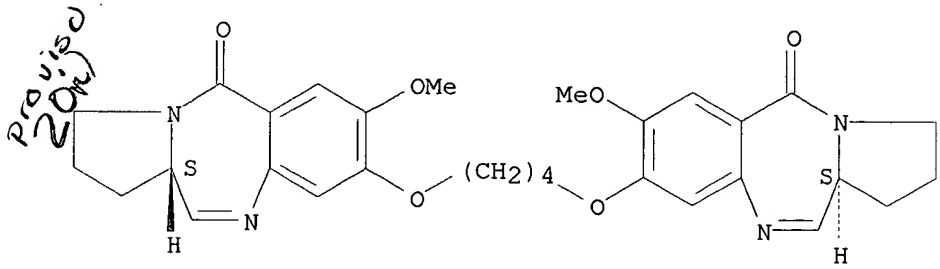
RN 187083-54-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,9-dichloro-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


Cl
N
H
S
N
Cl
O

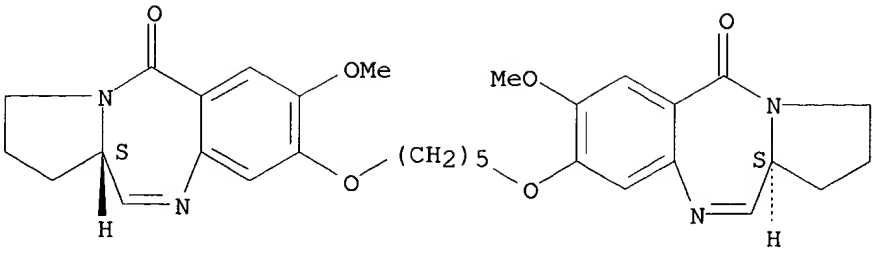
L26 ANSWER 29 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1996:644058 CAPLUS
DN 126:8088
TI Synthesis of Sequence-Selective C8-Linked Pyrrolo[2,1-c][1,4]benzodiazepine Interstrand DNA Crosslinking Agents
AU Thurston, David E.; Bose, D. Subhas; Thompson, Andrew S.; Howard, Philip W.; Leoni, Alberto; Croker, Stephen J.; Jenkins, Terrence C.; Neidle, Steven; Hartley, John A.; Hurley, Laurence H.
CS School of Pharmacy and Biomedical Science, University of Portsmouth, Portsmouth/Hants, PO1 2DT, UK
SO J. Org. Chem. (1996), 61(23), 8141-8147
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
AB An efficient convergent synthesis of a homologous series of C8-linked pyrrolobenzodiazepine dimers with remarkable DNA interstrand crosslinking activity and potent in vitro cytotoxicity is reported. The "amino thioacetal" cyclization procedure was used to produce the electrophilic DNA-interactive N10-C11 imine moiety during the final synthetic step. In order to construct the key A-ring fragments, a versatile convergent approach has been developed to join two units of vanillic acid with .alpha.,.omega.-dihaloalkanes of varying length to provide the required bis(4-carboxy-2-methoxyphenoxy)alkanes while avoiding the formation of mixts. of monoalkylated and bisalkylated products.
IT **145325-56-0P 145325-57-1P 145325-58-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 145325-56-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,4-butanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



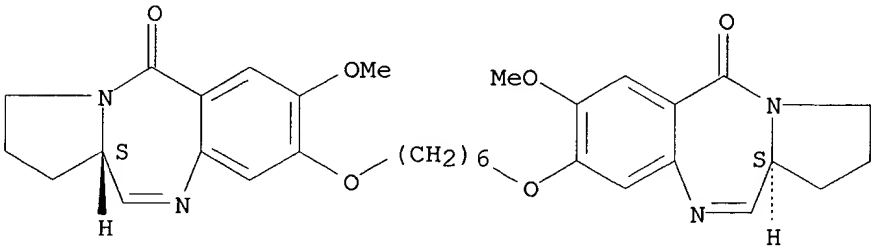
RN 145325-57-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



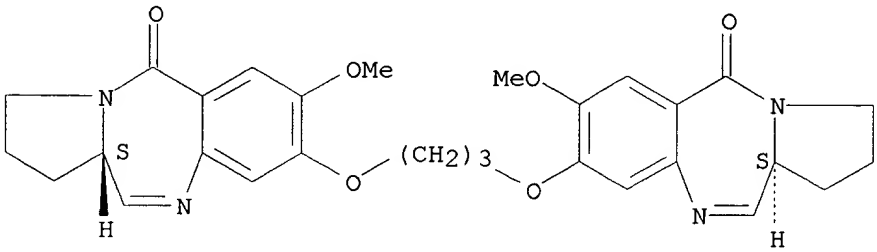
RN 145325-58-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,6-hexanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



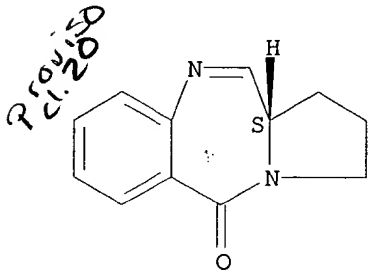
IT **140676-21-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of sequence-selective C8-Linked pyrrolobenzodiazepine interstrand DNA crosslinking agents)
RN 140676-21-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



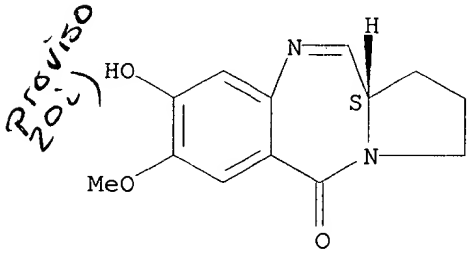
L26 ANSWER 30 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1996:575031 CAPLUS
DN 125:275482
TI Synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via azido reductive cyclization with HMDST
AU Kamal, Ahmed; Reddy, B. S. Praveen; Reddy, B. S. Narayan
CS Div. Org. Chem., Indian Inst. Chem. Technol., Hyderabad, 500 007, India
SO Tetrahedron Lett. (1996), 37(37), 6803-6806
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 125:275482
AB A new facile synthesis of pyrrolo[2,1-c][1,4]benzodiazepine ring system has been achieved by reductive cyclization of azide employing hexamethyldisilathiane (HMDST). The parent unsubstituted ring system and the natural product DC-81 have been prepd. in good overall yields.
IT **72435-89-3P 81307-24-6P**, DC-81 **182277-13-0P 182508-34-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of pyrrolobenzodiazepines by reductive cyclization of azide with hexamethyldisilathiane)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



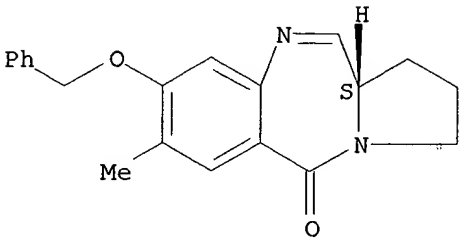
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



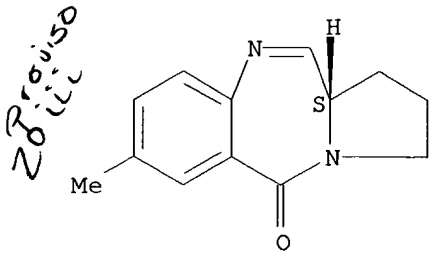
RN 182277-13-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl-8-(phenylmethoxy)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



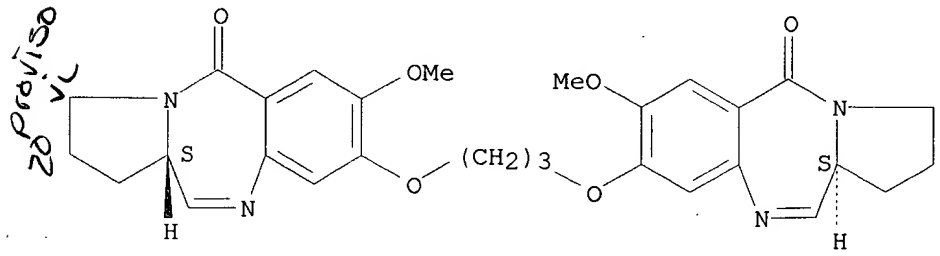
RN 182508-34-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



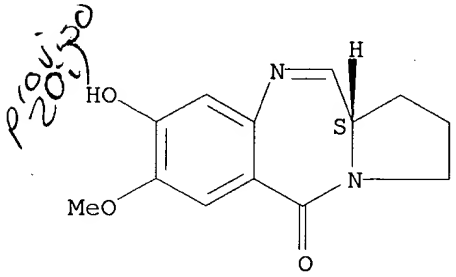
L26 ANSWER 31 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1996:550992 CAPLUS
DN 125:264974
TI Preclinical pharmacology and antitumor activity of the novel sequence-selective DNA minor-groove crosslinking agent DSB-120
AU Walton, M. I.; Goddard, P.; Kelland, L. R.; Thurston, D. E.; Harrap, K. R.
CS Institute Cancer Research, CRC Center Cancer Therapeutics, Belmont, SM2 5NG, UK
SO Cancer Chemother. Pharmacol. (1996), 38(5), 431-438
CODEN: CCPHDZ; ISSN: 0344-5704
DT Journal
LA English
AB In vitro cytotoxicity, antitumor activity, and preclin. pharmacokinetics of the novel sequence-selective, bifunctional alkylating agent DSB-120 (I), a synthetic pyrrolo[1,4][2,1-c]benzodiazepine dimer, was investigated. I was shown to be a potent cytotoxic agent against a panel of human colon carcinomas and two rodent tumors (L1210 and ADJ/PC6). The maximal antitumor effects were obsd. following a single i.v. dose but the therapeutic index was only 2.6. I was less effective when given i.p. either singly or by a daily x5 schedule. After a single i.v. dose at the max. tolerated dose the plasma elimination was biphasic, with a short distribution phase being followed by a longer elimination phase. Concns. of I in ADJ/PC6 tumors were very low, showing a peak of 0.4 .mu.gg at 5 min. The steady-state tumor/plasma ratio was about 5% and the AUC was only 2.5% of that occurring in the plasma. I appeared to be unstable in vivo, with only 1% of an administered dose being recovered unchanged in 24 h urine samples. Plasma protein binding was extensive at 96.6%. In conclusion, the poor antitumor activity of ,I may be a consequence of low tumor selectivity and drug uptake as a result of protein binding and/or extensive drug metab in vivo.
IT **140676-21-7**
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preclin. pharmacol. and antitumor activity of DNA minor-groove crosslinking agent DSB-120)
RN 140676-21-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



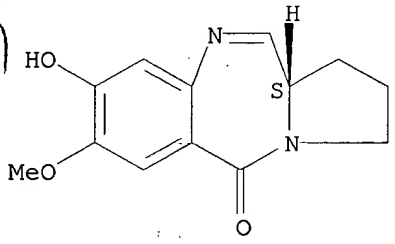
L26 ANSWER 32 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1996:490671 CAPLUS
DN 125:184902
TI Molecular mechanics study of the stereochemistry of formation of covalent pyrrolobenzodiazepine-DNA adducts
AU Adams, L. J.; Morris, S. J.; Banting, L.; Jenkins, T. C.; Thurston, D. E.
CS Cent. Molecular Design, Univ. Portsmouth, Portsmouth, PO1 2ED, UK
SO Pharm. Sci. (1995), 1(3), 151-154
CODEN: PHSCFB; ISSN: 1356-6881
DT Journal
LA English
AB The pyrrolobenzodiazepine (PBD) antitumor antibiotics are known to react at their C11-position with a no. of different nucleophiles, including DNA, to give a predominance of either C11(R) or C11(S) adducts, depending upon structural features such as the degree of satn. of the C-ring. This behavior has now been rationalized on the basis of mol. mechanics calcns.
IT **81307-24-6**, DC-81
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(mol. mechanics study of stereochem. of formation of covalent pyrrolobenzodiazepine-DNA adducts)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

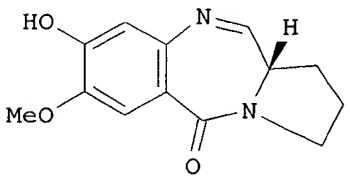


L26 ANSWER 33 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1996:380978 CAPLUS
DN 125:104253
TI DNA-binding properties of pyrrolo[2,1-c][1,4]benzodiazepine N10-C11 amidines
AU Foloppe, M. P.; Rault, S.; Thurston, D. E.; Jenkins, T. C.; Robba, M.
CS Cent. Etud. Rech. Medicament Normandie, Caen, 14032, Fr.
SO Eur. J. Med. Chem. (1996), 31(5), 407-410
CODEN: EJMCA5; ISSN: 0223-5234
DT Journal
LA English
AB A series of pyrrolo[2,1-c][1,4]benzodiazepine N10-C11 amidines has been evaluated for in vitro DNA binding through thermal denaturation studies. Some of these compds. cause a significant increase in melting for calf thymus DNA (e.g., 0.7.+-.0.1.degree.), possibly due to non-covalent interaction with bases positioned on the floor of the minor groove in the DNA duplex.
IT **81307-24-6**, DC-81
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA-binding properties of pyrrolo[2,1-c][1,4]benzodiazepine N10-C11 amidines)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 34 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1996:198494 CAPLUS
DN 124:316822
TI A new facile procedure for the preparation of pyrrolo[2,1-c][1,4]benzodiazepines: synthesis of the antibiotic DC-81 and its thio analog
AU Kamal, Ahmed; Reddy, B. S. Praveen; Reddy, B. S. Narayan
CS Div. Org. Chem., Indian Inst. Chem. Technol., Hyderabad, 500 007, India
SO Tetrahedron Lett. (1996), 37(13), 2281-4
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 124:316822
GI



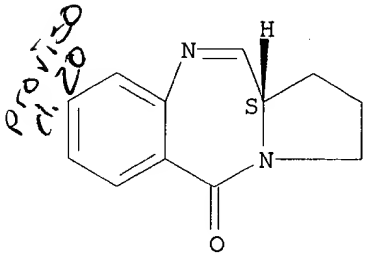
I

AB An efficient synthesis of the imine form of the pyrrolo[2,1-c][1,4]benzodiazepine ring system based on a new reductive cyclization procedure is described. The naturally occurring antibiotic DC-81 (I) and its 5-thio analog have also been synthesized to illustrate the usefulness of this methodol.

IT **72435-89-3P 81307-24-6P**, Antibiotic dc 81
127810-79-1P 175521-32-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of pyrrolo[2,1-c][1,4]benzodiazepines)

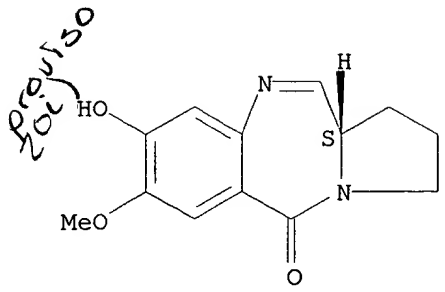
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



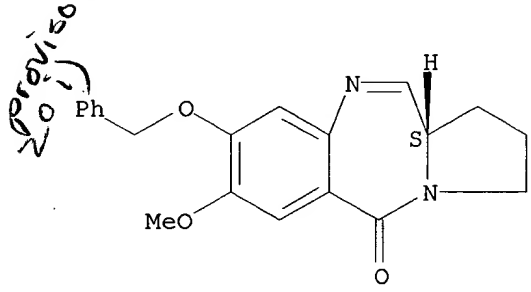
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



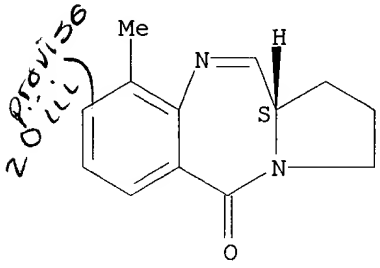
RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



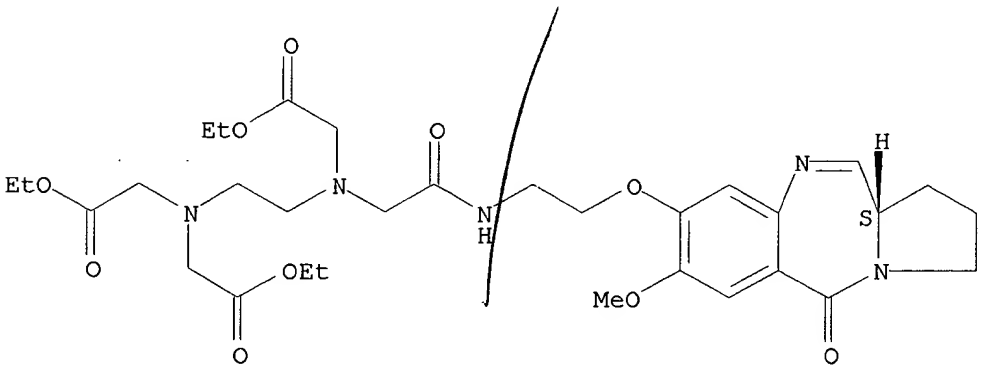
RN 175521-32-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



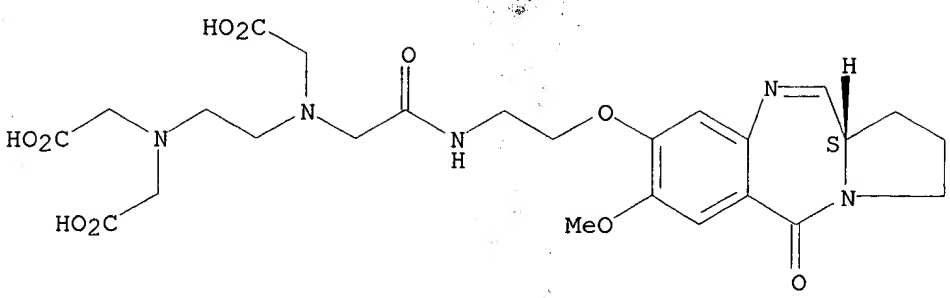
L26 ANSWER 35 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1996:158919 CAPLUS
DN 124:283579
TI Synthesis of a novel GC-specific covalent-binding DNA affinity-cleavage agent based on pyrrolobenzodiazepines (PDBs)
AU Thurston, David E.; Morris, Steven J.; Hartley, John A.
CS Sch. Pharmacy Biomedical Science, Univ. Portsmouth, Portsmouth, PO1 2DZ, UK
SO Chem. Commun. (Cambridge) (1996), (4), 563-5
CODEN: CHCOFS; ISSN: 1359-7345
DT Journal
LA English
AB Reported is the attachment of an EDTA moiety to DC-81, a member of the guanine(N2)-specific pyrrolobenzodiazepine family of antitumor antibiotics, to produce the first example of a covalent-binding GC-specific DNA-cleaving agent with a selectivity for 5'-PuGPu sequences (Pu = purine; G = guanine).
IT **175733-07-0P 175733-08-1DP**, iron complexes
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of GC-specific covalent-binding DNA affinity-cleavage agent based on pyrrolobenzodiazepines)
RN 175733-07-0 CAPLUS
CN Glycine, N-[2-[bis(2-ethoxy-2-oxoethyl)amino]ethyl]-N-[2-oxo-2-[[2-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]ethyl]amino]ethyl]-, ethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

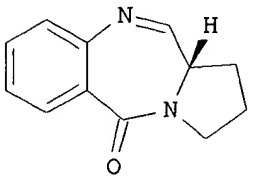


RN 175733-08-1 CAPLUS
CN Glycine, N-[2-[bis(carboxymethyl)amino]ethyl]-N-[2-oxo-2-[[2-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]ethyl]amino]ethyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 36 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1996:154392 CAPLUS
DN 124:289058
TI A new route for the synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via oxidation of cyclic secondary amine
AU Kamal, Ahmed; Rao, N. Venugopal
CS Indian Inst. Chem. Technol., Hyderabad, 500 007, India
SO Chem. Commun. (Cambridge) (1996), (3), 385-6
CODEN: CHCOFS; ISSN: 1359-7345
DT Journal
LA English
OS CASREACT 124:289058
GI



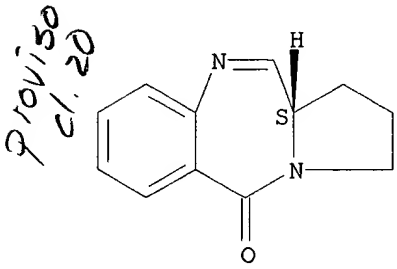
I

AB The synthesis of the imine-contg. pyrrolo[2,1-c][1,4]benzodiazepine DNA-binding antitumor antibiotics, e.g. I, was achieved by a new method of oxidn. of cyclic secondary amines which does not endanger the stereochem. integrity of the C-11a position.

IT **72435-89-3P 81307-24-6P 175521-32-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via oxidn. of cyclic secondary amines)

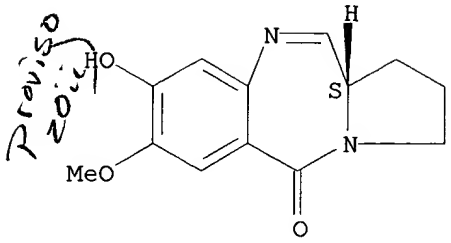
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



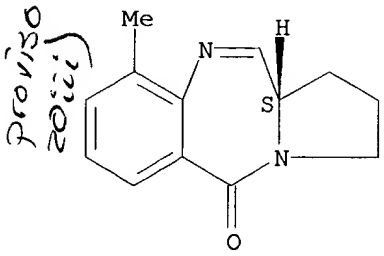
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

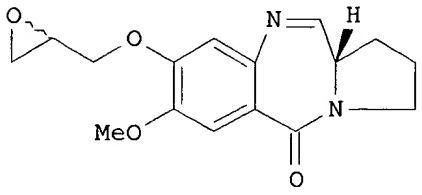


RN 175521-32-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 37 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1995:786320 CAPLUS
DN 124:8772
TI Design and synthesis of a novel epoxide-containing pyrrolo[2,1-c][1,4]benzodiazepine (PBD) via a new cyclization procedure
AU Wilson, Stuart C.; Howard, Philip W.; Thurston, David E.
CS Div. Med. Chem., Univ. Portsmouth, Portsmouth, Hants., PO1 2DZ, UK
SO Tetrahedron Lett. (1995), 36(35), 6333-6
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 124:8772
GI



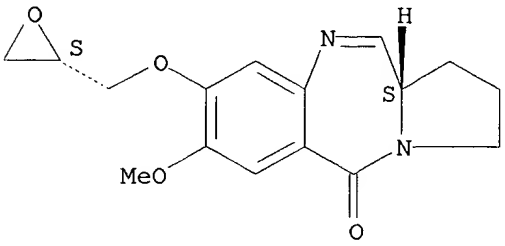
I

AB The synthesis of a potential DNA-crosslinking pyrrolo[2,1-c][1,4]benzodiazepine I substituted at the C8-position with a 2,3-epoxypropaneoxy moiety using a new cyclization procedure is described.

IT **171002-52-1P 171229-23-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(design and synthesis of a novel epoxide-contg. pyrrolobenzodiazepine via a new cyclization procedure)

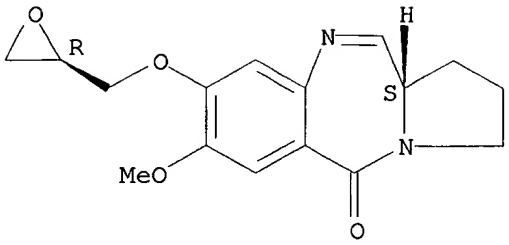
RN 171002-52-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-[(2S)-oxiranylmethoxy]-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



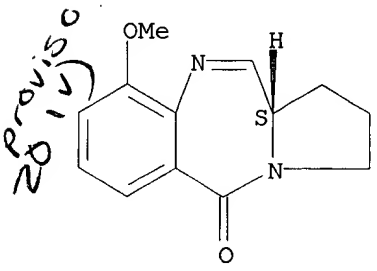
RN 171229-23-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(oxiranylmethoxy)-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

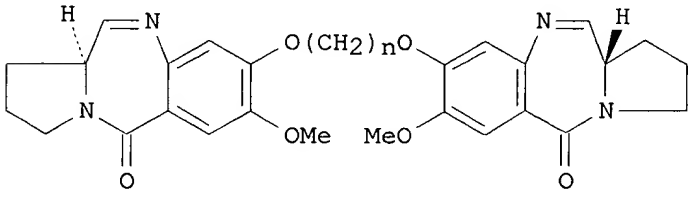

O
R
O
N
H
S
N
MeO
O

L26 ANSWER 38 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1995:730623 CAPLUS
DN 123:227886
TI A stereoselective synthesis of tilivalline and its analogs utilizing a new Mannich type intramolecular cyclization
AU Aoyama, Toyohiko; Shioiri, Takayuki
CS Fac. Pharm. Sci., Nagoya City Univ., Nagoya, 467, Japan
SO Yakugaku Zasshi (1995), 115(6), 446-59
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
OS CASREACT 123:227886
AB Tilivalline (I), a metabolite isolated from Klebsiella pneumoniae var. oxytoca, belongs to a group of pyrrolo[2,1-c][1,4]benzodiazepines, a characteristic skeleton of anthramycin-type antitumor antibiotics. The authors have accomplished a completely stereoselective, efficient and convenient synthesis of I utilizing a new Mannich type intramol. cyclization as a key step. Further, a computational chem. anal. clarified the effect of zinc chloride on the high stereoselectivity in the tilivalline synthesis. To aim both the extension of the scope of the new Mannich type intramol. cyclization and the studies on the structure-biol. activity relationship, the authors further extended the method to the synthesis of tilivalline derivs. and 2-(3'-indolyl)-1,4-benzodiazepines. Investigation on the cytotoxicity of I and its analogs has revealed that I shows the strong cytotoxicity toward mouse leukemia L 1210 cells and the replacement of the indole function of I with cyano one increases the cytotoxicity of I about 100 times (IC50 = 0.05 .mu.g/mL).
IT **110715-89-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(stereoselective synthesis of tilivalline and analogs utilizing a new Mannich type intramol. cyclization)
RN 110715-89-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 39 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1995:637534 CAPLUS
DN 123:285962
TI Facile and efficient synthesis of the dimers of DC-81 antitumor antibiotics
AU Kamal, Ahmed; Rao, N. Venugopal
CS Div. Org. Chem., Indian Inst. Chem. Technol., Hyderabad, 500 007, India
SO Tetrahedron Lett. (1995), 36(24), 4299-302
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 123:285962
GI



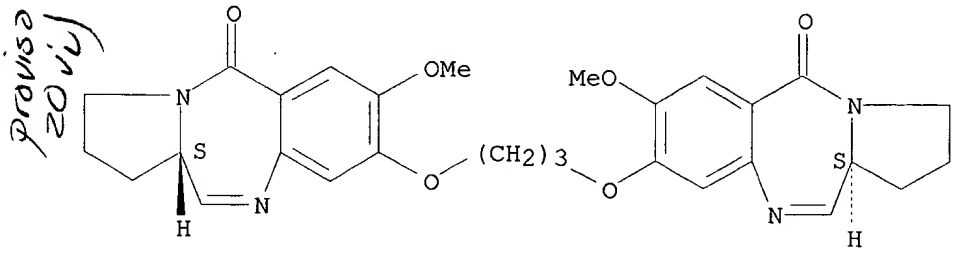
I

AB We report an improved, economical and versatile route to the dimers (I, n = 3, 4, 5) of DC-81 antitumor antibiotics. Particularly, the protection and deprotection steps in its synthesis and the prepn. of its precursors have been avoided. There is a significant improvement in the overall yields.

IT **169436-02-6P 169436-03-7P 169436-04-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of the dimers of DC-81 antitumor antibiotics)

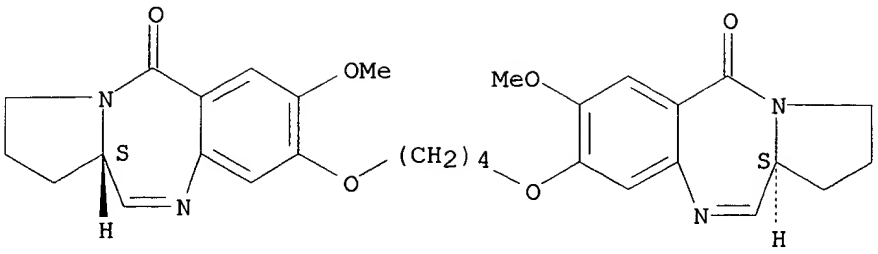
RN 169436-02-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



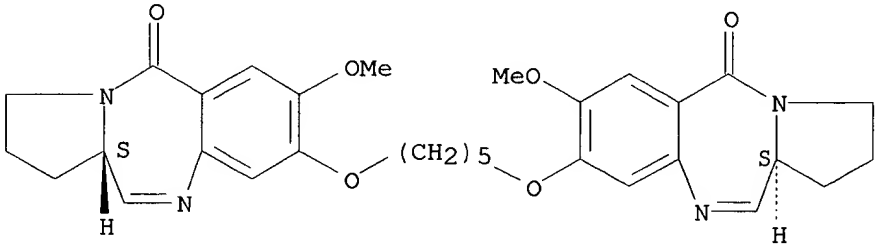
RN 169436-03-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,4-butanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 169436-04-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (R*,R*)- (9CI) (CA INDEX NAME)

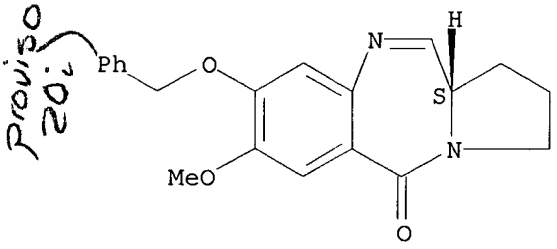
Relative stereochemistry.



09/763,767

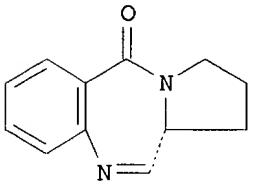
L26 ANSWER 40 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1995:629801 CAPLUS
DN 123:112029
TI Facile Synthesis of 1,4-Benzodiazepin-5-one Derivatives via Intramolecular Aza-Wittig Reaction. Application to an Efficient Synthesis of O-Benzyl DC-81
AU Eguchi, Shoji; Yamashita, Keizo; Matsushita, Yuji; Kakehi, Akikazu
CS Faculty of Engineering, Nagoya University, Nagoya, 464-01, Japan
SO J. Org. Chem. (1995), 60(13), 4006-12
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
AB The tandem Staudinger/aza-Wittig reaction of N-(o-azidobenzoyl)-.alpha.-amino acid esters gave the corresponding 1,4-benzodiazepin-5-one derivs. in moderate to good yields. This method was applied successfully to a new efficient synthesis of BzlDC-81.
IT **127810-79-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(facile synthesis of benzodiazepinone derivs. via tandem Staudinger/aza-Wittig reaction)
RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

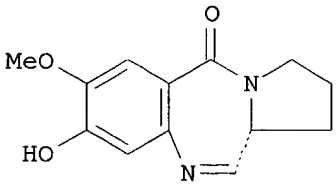


Proviso 20%

L26 ANSWER 41 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1995:567326 CAPLUS
DN 123:143505
TI Synthesis of pyrrolo[2,1-c][1,4]benzodiazepines via an intramolecular aza-Wittig reaction. Synthesis of the antibiotic DC-81
AU Molina, Pedro; Diaz, Isidora; Tarraga, Alberto
CS Facultad Quimicas, Universidad Murcia, Murcia, E-30071, Spain
SO Tetrahedron (1995), 51(19), 5617-30
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
GI



I



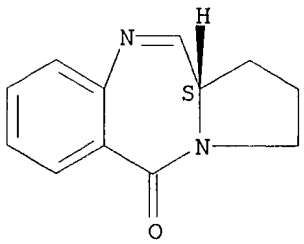
II

AB A new and efficient synthesis of the pyrrolo[2,1-c][1,4]benzodazepine (PBD) ring system has been carried out using, as a key step, an intramol. aza Witting reaction of the appropriately substituted N-(2-azidobenzoyl)pyrrolidine-2-carboxaldehydes. The parent unsubstituted PBD I and the natural product DC-81 II have been prepd. in the imine form in good overall yields.

IT **72435-89-3P 81307-24-6P**, DC 81 **127810-79-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of pyrrolobenzodiazepines and DC-81 via intramol. aza-Wittig)

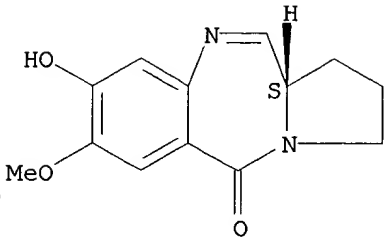
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

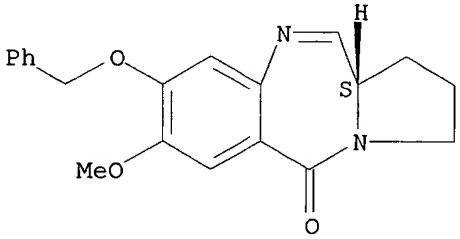
Absolute stereochemistry.



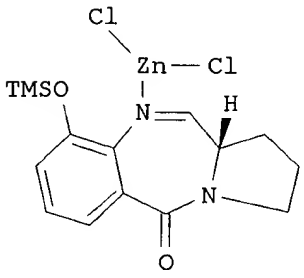
Prov/so 20:1

RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L26 ANSWER 42 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1995:213595 CAPLUS
DN 122:56290
TI Effect of zinc halides on the high stereoselectivity of a new Mannich type cyclization in the tilivalline synthesis. A computational chemical analysis
AU Matsumoto, Takatoshi; Aoyama, Toyohiko; Shioiri, Takayuki; Osawa, Eiji
CS Dep. Synthetic Org. Chem., Nagoya City Univ., Nagoya, 467, Japan
SO Tetrahedron (1994), 50(32), 9775-80
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
GI



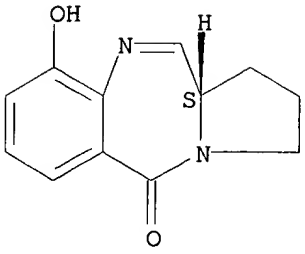
I

AB The calcn. by the semi-empirical MO method concerning the effect of zinc halides on the high stereoselectivity of a new Mannich type cyclization in our tilivalline synthesis has revealed that (1) zinc chloride coordinates with the N10 atom during the reaction and (2) the steric hindrance on the .alpha. side and the extension of LUMO to the .beta. side in the intermediate I govern the high stereoselectivity.

IT **71444-83-2 110715-89-4 160094-61-1**
160094-62-2 160094-63-3 160094-64-4
160094-65-5 160094-66-6 160094-67-7
160117-37-3 160117-38-4 160117-39-5
160117-40-8 160117-41-9 160117-42-0
160117-43-1 160117-44-2 160117-45-3
160117-46-4 160117-47-5 160117-48-6
160117-49-7
RL: PRP (Properties)
(MO calcns. on the effect of zinc halides on the stereoselectivity of a Mannich type cyclization in the tilivalline synthesis)

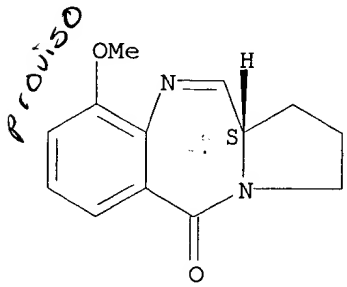
RN 71444-83-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



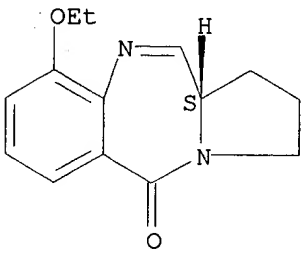
RN 110715-89-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



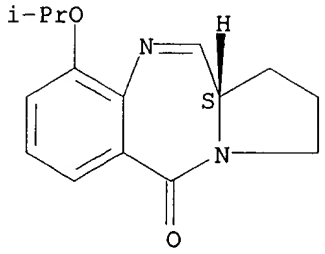
RN 160094-61-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-ethoxy-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



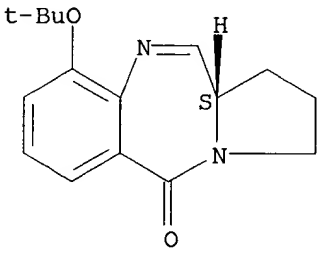
RN 160094-62-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-(1-methylethoxy)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



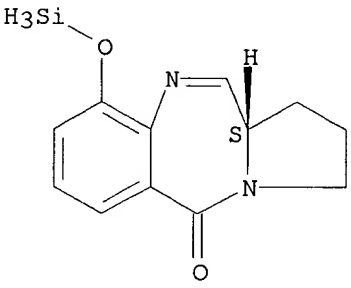
RN 160094-63-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-(1,1-dimethylethoxy)-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



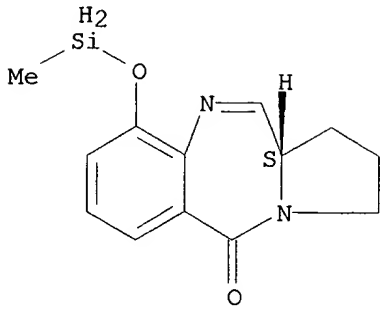
RN 160094-64-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-(silyloxy)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



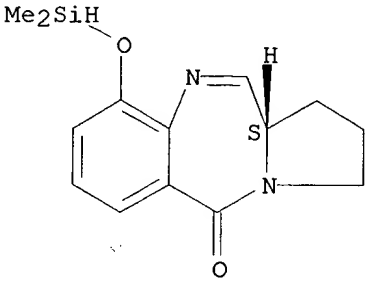
RN 160094-65-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-[(methylsilyl)oxy]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



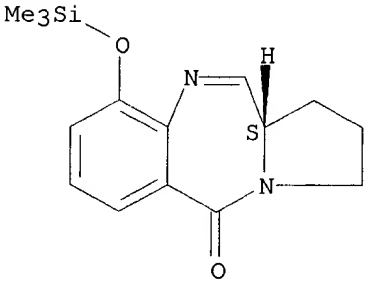
RN 160094-66-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-[(dimethylsilyl)oxy]-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

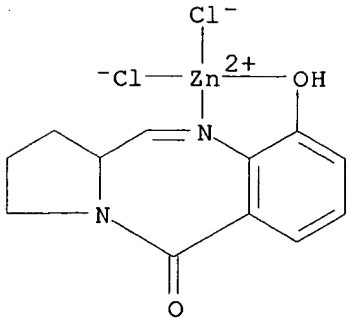


RN 160094-67-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-, (S)- (9CI) (CA INDEX NAME)

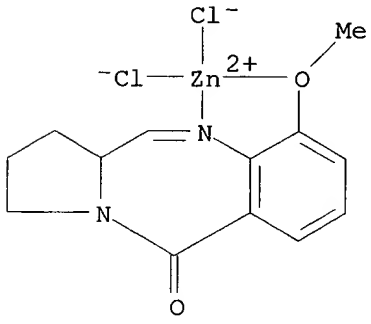
Absolute stereochemistry.



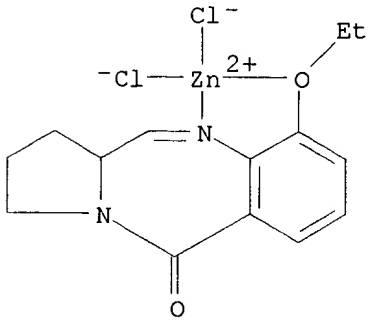
RN 160117-37-3 CAPLUS
CN Zinc, dichloro(1,2,3,11a-tetrahydro-9-hydroxy-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9)-, [T-4-(S)]- (9CI) (CA INDEX NAME)



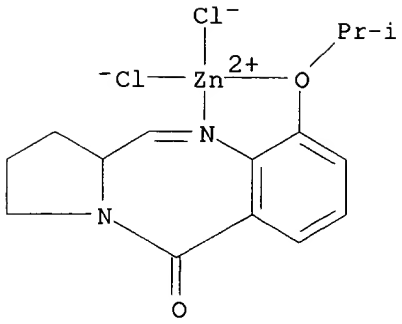
RN 160117-38-4 CAPLUS
CN Zinc, dichloro(1,2,3,11a-tetrahydro-9-methoxy-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9)-, [T-4-(S)]- (9CI) (CA INDEX NAME)



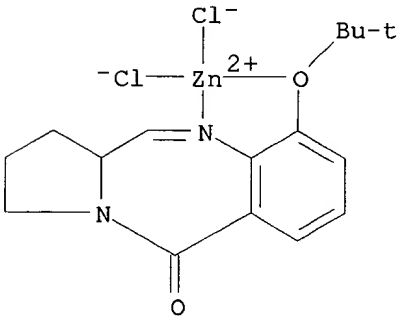
RN 160117-39-5 CAPLUS
CN Zinc, dichloro(9-ethoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9)-, [T-4-(S)]- (9CI) (CA INDEX NAME)



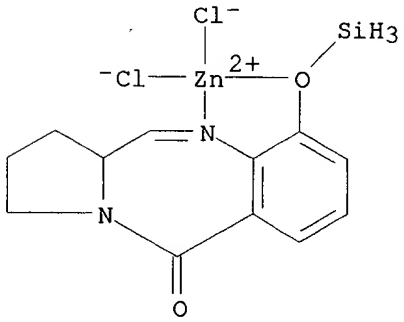
RN 160117-40-8 CAPLUS
CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-(1-methylethoxy)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



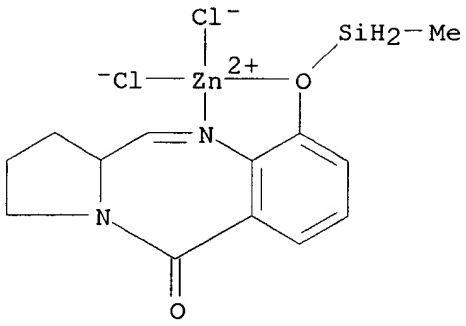
RN 160117-41-9 CAPLUS
CN Zinc, dichloro[9-(1,1-dimethylethoxy)-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



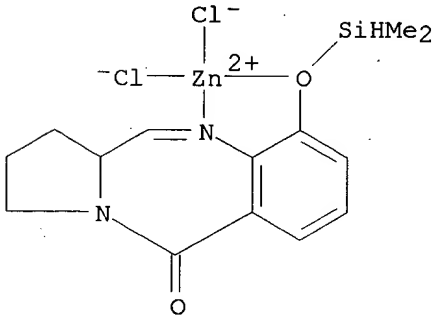
RN 160117-42-0 CAPLUS
CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-(silyloxy)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



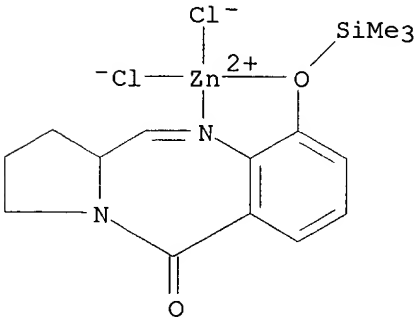
RN 160117-43-1 CAPLUS
CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-[(methylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



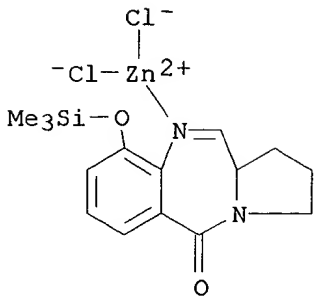
RN 160117-44-2 CAPLUS
CN Zinc, dichloro[9-[(dimethylsilyl)oxy]-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



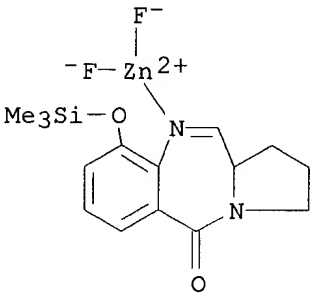
RN 160117-45-3 CAPLUS
CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



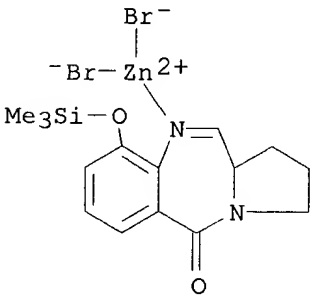
RN 160117-46-4 CAPLUS
CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10]-, (S)- (9CI) (CA INDEX NAME)



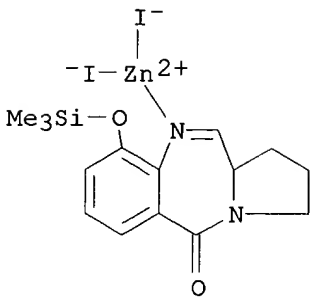
RN 160117-47-5 CAPLUS
CN Zinc, difluoro[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10]-, (S)- (9CI) (CA INDEX NAME)



RN 160117-48-6 CAPLUS
CN Zinc, dibromo[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10]-, (S)- (9CI) (CA INDEX NAME)



RN 160117-49-7 CAPLUS
CN Zinc, diiodo[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10]-, (S)- (9CI) (CA INDEX NAME)


I⁻
⁻I—Zn²⁺
Me₃Si—O
N
N
O

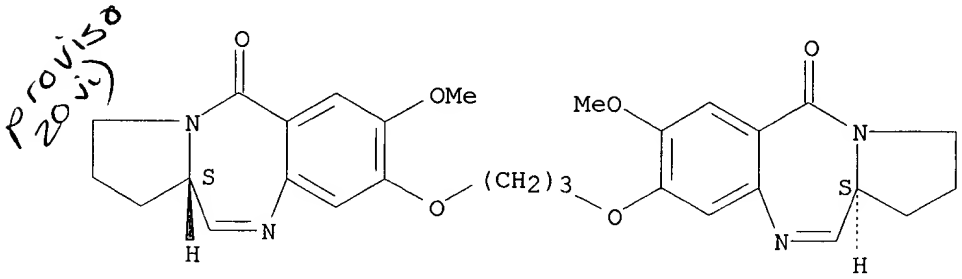
09/763,767

L26 ANSWER 43 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1995:107251 CAPLUS
DN 122:97894
TI DNA damage by anticancer agents and its repair: mapping in cells at the subgene level with quantitative polymerase chain reaction
AU Grimaldi, Keith A.; Bingham, John P.; Souhami, Robert L.; Hartley, John A.
CS Dep. Oncology, Univ. Coll. Long Med. Sch., London, W1P 8BT, UK
SO Anal. Biochem. (1994), 222(1), 236-42
CODEN: ANBCA2; ISSN: 0003-2697
DT Journal
LA English
AB The quant. polymerase chain reaction (QPCR)-based assay was used to measure DNA damage and repair to a small (523 bp) fragment of the single-copy human N-ras gene in K562 cells. Compared with previous methods DNA prepn. from treated cells and the subsequent detection of the radioactive product were considerably simplified. The results demonstrated that QPCR can be used to measure damage in a small gene segment, caused by cisplatin, nitrogen, and quinacrine mustards. Drug-DNA adducts produced by two novel minor groove binding, sequence-specific mols. (AT-486 and DSB-120) could be detected at physiol. relevant concns. of drug. For both cis-platin and nitrogen mustard the concn. required to cause damage in cells were higher than those needed to cause equiv. damage in isolated DNA. In contrast both AT-488 and quinacrine mustard caused more damage at equimolar concns. in cells than in isolated DNA. DSB-120, which is closely related to AT-486, was found to be 15-fold less effective than the latter at causing damage in treated cells despite similar reactivity with isolated DNA. Repair of damage caused by quinacrine mustard to the same small gene fragment was found to proceed at a const. rate over 24 h. The QPCR assay presented here is a simple quant. method to measure damage and repair in subgene functional units such as promoters, introns, and exons.
IT **160675-00-3**, DSB 120
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(drug-DNA adducts produced by two novel minor groove binding, sequence-specific mols. (AT-486 and DSB-120) could be detected at physiol. relevant concns. of drug by quant. PCR)
RN 160675-00-3 CAPLUS

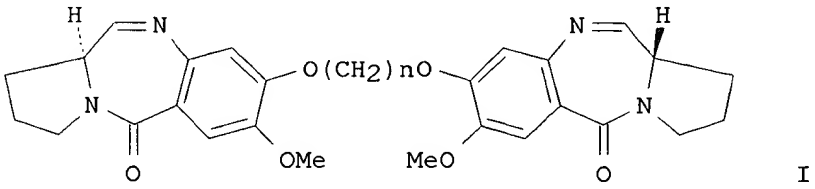
Provisional 20 Jun

L26 ANSWER 44 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1995:50719 CAPLUS
DN 122:99738
TI Development of anthramycin-based sequence-selective DNA crosslinking agents
AU Jenkins, Terence C.; Neidle, Stephen; Thurston, David E.
CS Cancer Res. Campaign Biomolecular Structure Unit, Inst. Cancer Res., Sutton/Surrey, SM2 5NG, UK
SO Chem. Heterocycl. Compd., Proc. Symp., 11th (1993), 173-9. Editor(s): Stibor, Ivan. Publisher: Prague Inst. Chem. Technol., Prague, Czech. CODEN: 60BQAT
DT Conference
LA English
AB Mol. modeling techniques, using double-stranded DNA as a template, have been used to design a series of potent and novel DNA crosslinking agents with useful G/C recognition properties. DNA reactivity has been confirmed using biophys. and biochem. assays, and qual. structure-activity correlations for cytotoxic potency have been demonstrated. NMR soln. studies provide a rational basis for the reactivity and DNA-crosslinking efficiency of the most reactive pyrrolobenzodiazepine dimer homolog, DSB-120. The predicted d(GATC) sequence preference for this agent, where the sequence contains a spanned ApT base tract, is substantiated by facile adduct formation with d(CICGATCICG).
IT **140676-21-7**
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study)
(pyrrolobenzodiazepine dimer homolog; development of anthramycin-based sequence-selective DNA crosslinking agents)
RN 140676-21-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 45 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1994:671426 CAPLUS
DN 121:271426
TI Cellular pharmacology of novel C8-linked anthramycin-based sequence-selective DNA minor groove cross-linking agents
AU Smellie, M.; Kelland, L.R.; Thurston, D.E.; Souhami, R.L.; Hartley, J.A.
CS School, UCL Medical, London, W1P 8BT, UK
SO Br. J. Cancer (1994), 70(1), 48-53
CODEN: BJCAAI; ISSN: 0007-0920
DT Journal
LA English
GI



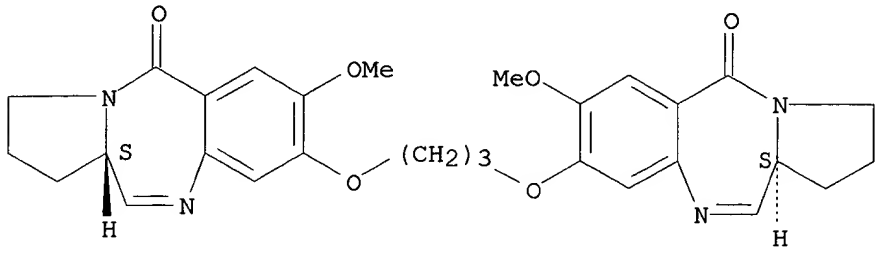
I

AB The cellular pharmacol. of a series of C8-linked pyrrolobenzodiazepine dimers with polymethylene linkers I (n = 3-6) has been studied in a range of human tumor cell lines. The four compds. showed the same pattern of relative activity in five ovarian carcinoma cell lines and one cervical carcinoma cell line, which correlated with the previously demonstrated DNA interstrand crosslinking ability of the compds. in plasmid DNA. In human leukemic K562 cells the agents produced a block in the G2/M phase of the cell cycle characteristic of crosslinking drugs, and extensive interstrand crosslinking was obsd. in cells by alk. elution with no evidence of single-strand breaks. Cross-links continued to increase up to 24 h following a 1 h exposure to drug, and no repair was evident by 48 h. In a series of ovarian and cervical carcinoma cell lines with acquired resistance to cisplatin no cross-resistance to the most potent compd. I (n = 3) was obsd. in two lines whose major mechanism of resistance to cisplatin was reduced platinum transport. Cross-resistance to 1 was obsd. in a cell line (A2780cisR) possessing elevated glutathione, and depletion of intracellular glutathione using D,L-buthionine-S,R-sulfoximine (BSO) from 10.25 nmol to 2.8 nmol 10-6 cells reduced the level of resistance from 11-fold to 2-fold compared with sensitive cells. Crosslinking in the resistant cells was restored to 80% of the level in the parent line by BSO pretreatment. There was also a correlation between glutathione levels and sensitivity to 1 measured in several other ovarian cell lines. I (n = 3) also showed cross-resistance in the doxorubicin-resistance cell line 41MdoxR and partial cross-resistance in CHldoxR cells. Both these lines possess elevated levels of p170 glycoprotein. Following treatment with 6 .mu.M verapamil, the resistance in these lines decreased almost 2-fold and 8-fold resp.

IT **140676-21-7 145325-56-0 145325-57-1 145325-58-2**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cellular pharmacol. of novel C8-linked anthramycin-based sequence-selective DNA minor groove crosslinking agents)
RN 140676-21-7 CAPLUS

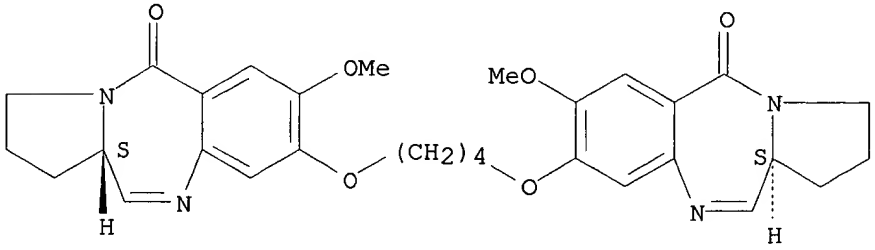
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



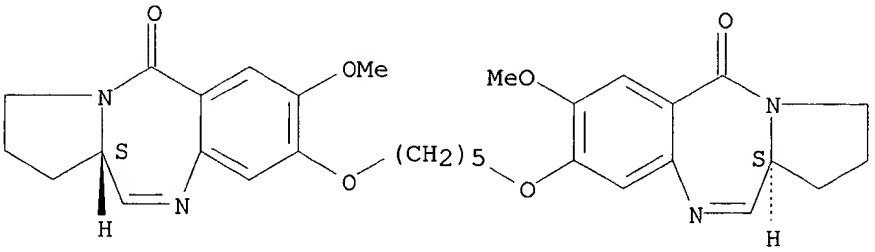
RN 145325-56-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,4-butanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



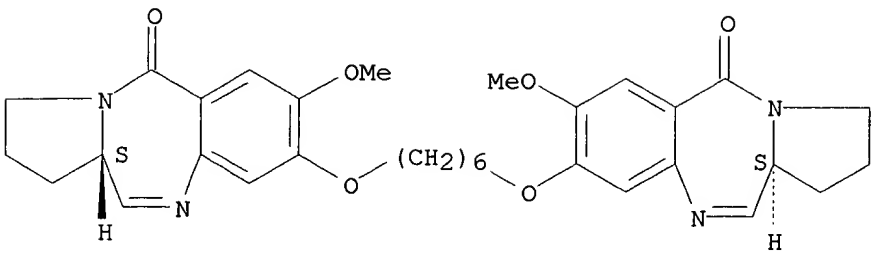
RN 145325-57-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



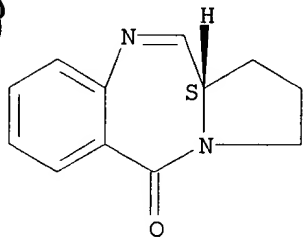
RN 145325-58-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,6-hexanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 46 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1994:528030 CAPLUS
DN 121:128030
TI Synthesis, DNA binding and crosslinking studies of pyrrolo[1,4]benzodiazepine dimers
AU Zhang, Jundong
CS Brown Univ., Providence, RI, USA
SO (1993) 204 pp. Avail.: Univ. Microfilms Int., Order No. DA9407069
From: Diss. Abstr. Int. B 1994, 54(10), 5159
DT Dissertation
LA English
AB Unavailable
IT **72435-89-3DP**, dimers
RL: PREP (Preparation)
(synthesis and DNA binding and crosslinking studies of)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L26 ANSWER 47 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1994:270468 CAPLUS
DN 120:270468
TI Anticancer pyrrolo[2,1-c][1,4]benzodiazepines
IN Thurston, David Edwin; Bose, Deverakonda Subhas
PA Cancer Research Campaign Technolgy Ltd., UK
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9318045	A1	19930916	WO 1993-GB483	19930308
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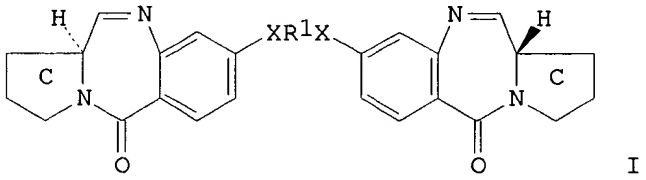
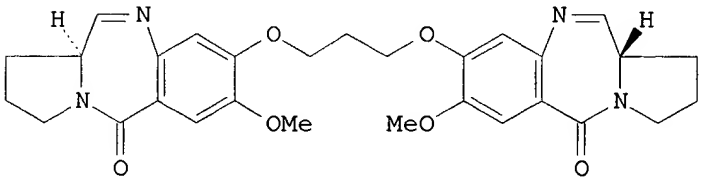
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9301637	A	19931004	ZA 1993-1637	19930308
	AU 9336435	A1	19931005	AU 1993-36435	19930308
PRAI	GB 1992-5051		19920309		
	WO 1993-GB483		19930308		

OS MARPAT 120:270468
GI



I



II

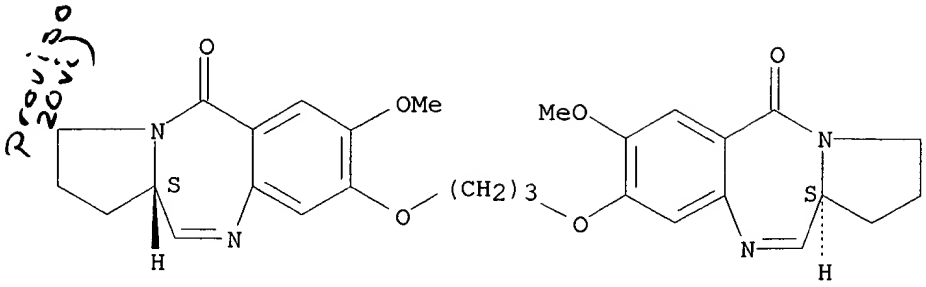
AB The title compds. I [R1 = (un)substituted C3-12 alkylene; X = O, S, NH; the pyrrolobenzodiazepine ring may contain addnl. substituents in .gtoreq.1 of the 1, 2, 3, 6, 7, 9, and 11 positions and the C rings may optionally contain .gtoreq.1 addnl. hetero ring atom], which are capable of crosslinking double-stranded DNA and which are useful as anticancer agents, are prepd. Thus, pyrrolobenzodiazepine II, prepd. from vanillic acid in 7 steps, demonstrated 50% inhibitory concn. against L1210 mouse leukemia cells of 0.01 .mu.M and against ADJ/PC6 mouse plasma plasmacytoma of 0.0005 .mu.M.

IT **140676-21-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and anticancer activity of)

RN 140676-21-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

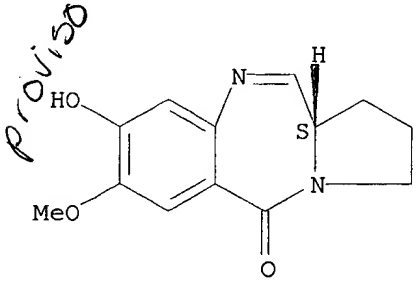


See SO 8 of 107

09/763,767

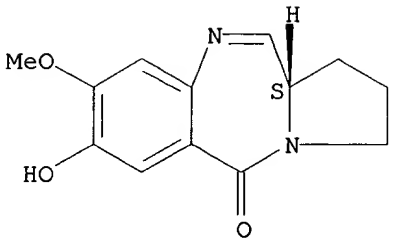
L26 ANSWER 48 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1994:235228 CAPLUS
DN 120:235228
TI A quantitative assay to measure the relative DNA-binding affinity of pyrrolo[2,1-c][1,4]benzodiazepine (PBD) antitumor antibiotics based on the inhibition of restriction endonuclease BamHI
AU Puvvada, Madhu S.; Hartley, John A.; Jenkins, Terence C.; Thurston, David E.
CS Sch. Pharm. Biomed. Sci., Univ. Portsmouth, Portsmouth, PO1 2DZ, UK
SO Nucleic Acids Res. (1993), 21(16), 3671-5
CODEN: NARHAD; ISSN: 0305-1048
DT Journal
LA English
AB An assay has been developed (restriction endonuclease digestion assay-RED100) based on inhibition of the restriction endonuclease BamHI that is capable of quant. evaluation of the relative DNA-binding affinity of pyrrolo[2,1-c][1,4]benzodiazepine (PBD) antitumor antibiotics. This method provides comparable results to those obtained from thermal denaturation and ethidium bromide displacement assays but is much more sensitive, discriminating between mols. of similar structure such as DC-81, iso-DC-81 and neothramycin. The results reveal a trend between relative DNA-binding affinity and in vitro cytotoxicity for the PBDs in two tumor cell lines studied.
IT **81307-24-6**, DC 81 **147778-99-2**, Iso-DC 81
RL: PRP (Properties)
(DNA binding affinity of, assay for, cytotoxicity in relation to)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

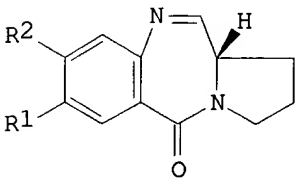


RN 147778-99-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-hydroxy-8-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

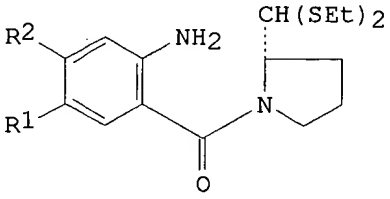
Absolute stereochemistry. Rotation (+).


MeO
HO
N
H
S
N
O

L26 ANSWER 49 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1994:30583 CAPLUS
DN 120:30583
TI A new convenient procedure for the synthesis of pyrrolo[2,1-c][1,4]benzodiazepines
AU Courtney, Stephen M.; Thurston, David E.
CS Sch. Pharm. Biomed. Sci., Univ. Portsmouth, Portsmouth/Hants, PO1 2DZ, UK
SO Tetrahedron Lett. (1993), 34(33), 5327-8
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 120:30583
GI



I



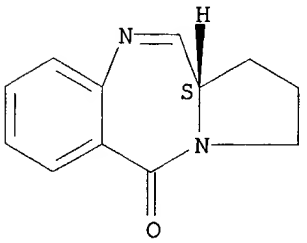
II

AB An efficient synthesis of the pyrrolo[2,1-c][1,4]benzodiazepine (PDB) ring system based on a new cyclization procedure is reported. The parent unsubstituted PDB I (R1 = R2 = H) and the benzyl deriv. I (R1 = OMe, R2 = OCH2Ph) of the natural product DC-81 I (R1 = MeO, R2 = OH) have been synthesized to illustrate the utility of this procedure. Thus, amino dithioacetals II were prepd. and treated with SO2Cl2/SiO2/CH2Cl2 to give I (R1 = R2 = H; R1 = OMe, R2 = OCH2Ph).

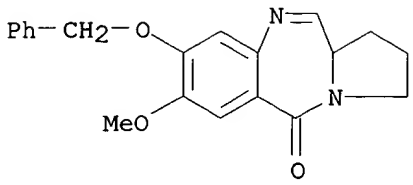
IT **72435-89-3P 151512-29-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

Proviso cl. 20

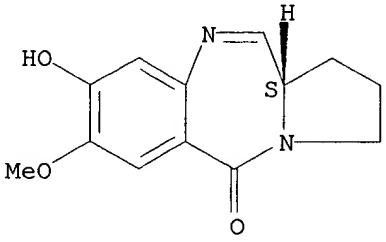


RN 151512-29-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)- (9CI) (CA INDEX NAME)

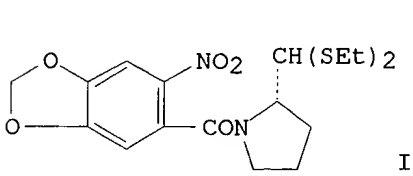


IT **81307-24-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of unsubstituted and benzyl derivs.)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

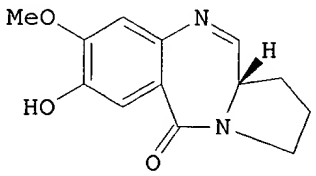
Absolute stereochemistry.



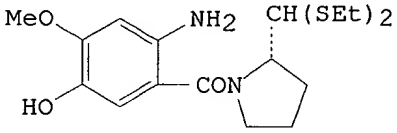
L26 ANSWER 50 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1993:254878 CAPLUS
DN 118:254878
TI Tin dichloride-induced regiospecific opening of the 1,3-benzodioxole ring system: a route to the novel DNA-interactive ligand iso-DC-81
AU Bose, D. Subhas; Thurston, David E.
CS Sch. Pharm. Biomed. Sci., Univ. Portsmouth, Portsmouth, PO1 2DZ, UK
SO Tetrahedron Lett. (1993), 34(8), 1377-8
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 118:254878
GI



I



II

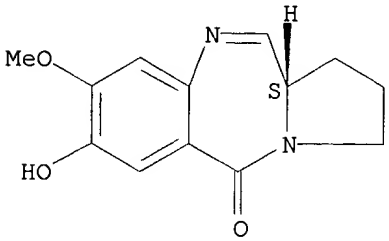


III

AB A novel tin-catalyzed regiospecific cleavage of a 1,3-benzodioxole ring system I is reported that has been applied to the synthesis of a uniquely substituted DNA-binding pyrrolo[2,1-c][1,4]benzodiazepine antitumor agent, iso-DC-81 (II). Thus, I was treated with SnCl2 in MeOH to give aminohydroxymethoxybenzamide III, which was cyclized with HgCl2 and CaCO3 in MeCN-H2O to give II.

IT **147778-99-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., DNA-binding, and cytotoxicity of)
RN 147778-99-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-hydroxy-8-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

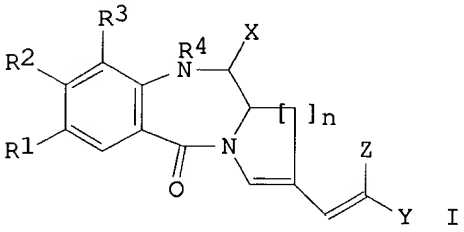
Absolute stereochemistry. Rotation (+).



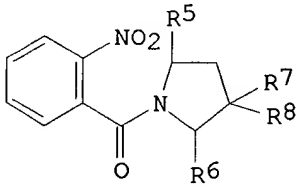
L26 ANSWER 51 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1993:147588 CAPLUS
DN 118:147588
TI Preparation of pyrrolo[1,4]benzodiazepines as antibiotics and antitumor agents
IN Langlois, Nicole; Favre, Florence; Tempete-Gaillourdet, Christiane; Werner, Georges Hubert
PA Centre National de la Recherche Scientifique, Fr.
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9219620	A1	19921112	WO 1992-FR410	19920506
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
FR 2676230	A1	19921113	FR 1991-5636	19910507
FR 2676230	B1	19930827		
PRAI FR 1991-5636		19910507		

OS MARPAT 118:147588
GI



I



II

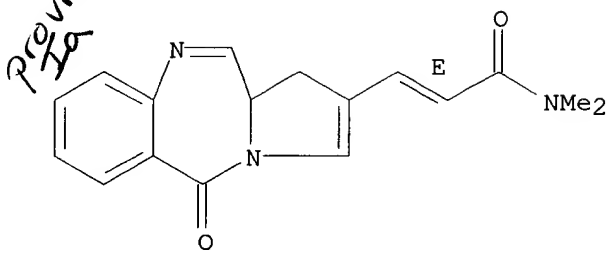
AB Title compds. (I; R1-R3 = H, halo, OH, alkoxy, etc.; R1 may addnl. = O-1'-sibrosamine; R4 = H, alkyl, alkanoyl; X = H, OH, alkoxy, NH2, etc.; R4X = bond; Y, Z = H, alkyl, alkoxycarbonyl, CONH2, etc.; R4X = bond; Y, Z = H, alkyl, alkoxycarbonyl, CONH2, etc.; n = 1 or 2) were prepd. Thus, nitrobenzamide II (R5 = CH2OAc, R6 = OMe, R7 = R8 = H) was converted in 5 steps to II (R5 = CHO, R6R7 = bond, R8 = CH:CHCONMe2) which was cyclized to give I (R1-R3 = Z = H, Y = CONMe2, n = 1) (III; R4X = bond). III (R4 = H, X = OMe) had MIC of .apprx. 60 mg/mL against Staphylococcus.

IT **146374-66-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antibiotic and antitumor agent)

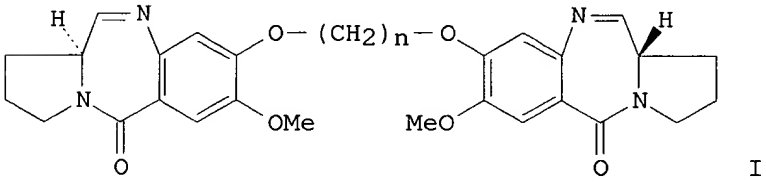
RN 146374-66-5 CAPLUS
CN 2-Propenamide, 3-(5,11a-dihydro-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)-N,N-dimethyl-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

Proviso Ia



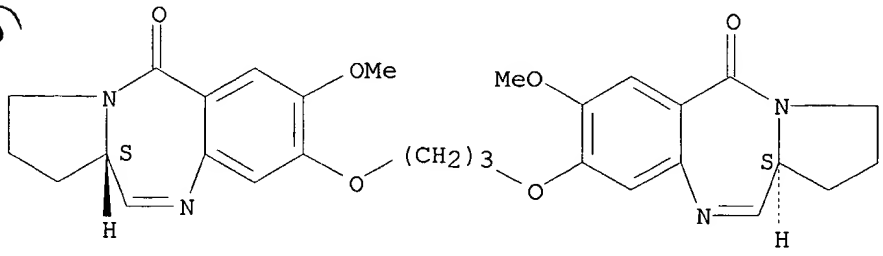
L26 ANSWER 52 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1993:59681 CAPLUS
DN 118:59681
TI Effect of linker length on DNA-binding affinity, cross-linking efficiency and cytotoxicity of C8-linked pyrrolobenzodiazepine dimers
AU Bose, D. Subhas; Thompson, Andrew S.; Smellie, Melissa; Berardini, Mark D.; Hartley, John A.; Jenkins, Terence C.; Neidle, Stephen; Thurston, David E.
CS Sch. Pharm. Biomed. Sci., Univ. Portsmouth, Portsmouth, PO1 2DZ, UK
SO J. Chem. Soc., Chem. Commun. (1992), (20), 1518-20
CODEN: JCCCAT; ISSN: 0022-4936
DT Journal
LA English
OS CASREACT 118:59681
GI



I

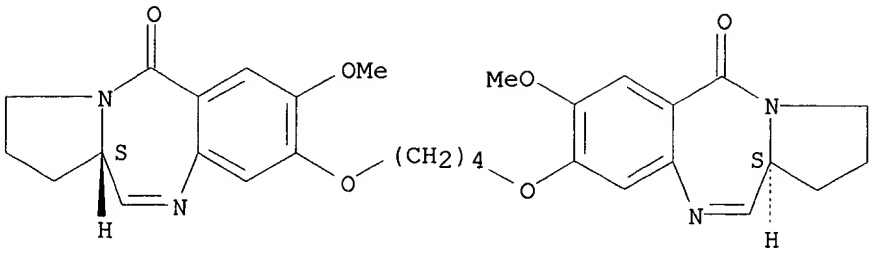
AB An efficient synthesis of a homologous series of C8-linked pyrrolobenzodiazepine dimers I (n = 3-6) in 8 steps starting from vanillic acid is reported. I (n = 3, 5), with an odd no. of methylenes in the linker show a higher affinity for DNA, enhanced crosslinking efficiency, and are more cytotoxic compared with I (n = 4, 6).
IT **140676-21-7P 145325-56-0P 145325-57-1P 145325-58-2P**
RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and binding with DNA and cytotoxicity of)
RN 140676-21-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



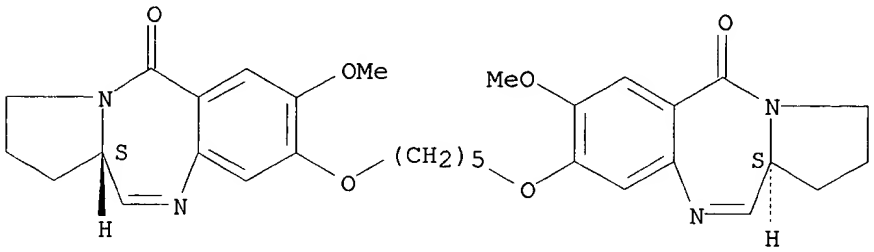
RN 145325-56-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,4-butanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



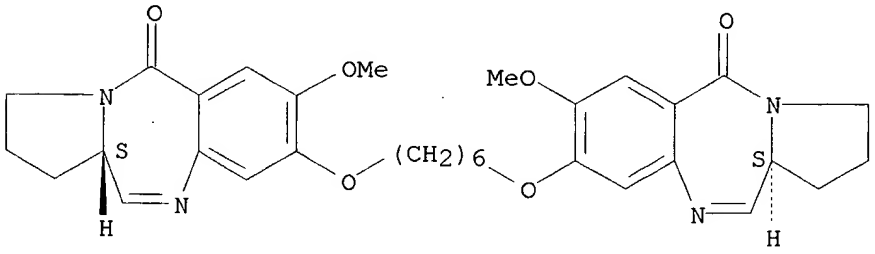
RN 145325-57-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



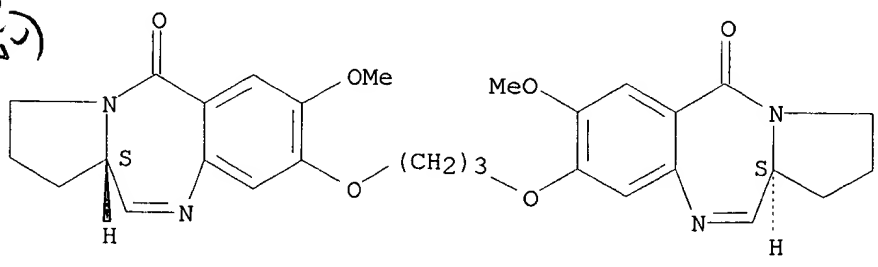
RN 145325-58-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,6-hexanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

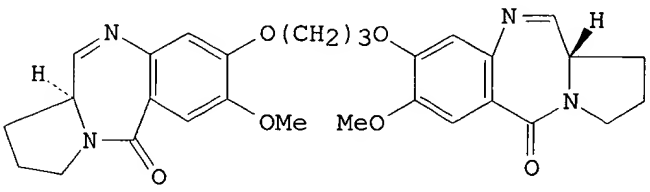


L16 ANSWER 53 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1992:483006 CAPLUS
DN 117:83006
TI Template-directed design of a DNA-DNA crosslinker based upon a bis-tomaymycin-duplex adduct
AU Wang, Jeh Jeng; Hill, G. Craig; Hurley, Laurence H.
CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA
SO J. Med. Chem. (1992), 35(16), 2995-3002
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB A template-directed approach to the design of a DNA-DNA interstrand cross-linker based upon the structure of a bis-tomaymycin-duplex adduct has been carried out. Tomaymycin is a member of the pyrrolo[1,4]benzodiazepines antitumor antibiotics. In a previous study it was shown that two tomaymycin mols. can be covalently bound to a 12-mer duplex mol., where the drug mols. are on opposite strands six base-pairs apart, and the stereochem. at the drug bonding site, and orientation in the minor groove, was defined by high-field NMR. This bis-tomaymycin 12-mer duplex adduct maintains the self-complementarity of the duplex and a B-type structure. In the present study it was shown using high-field NMR that this same 12-mer sequence can be truncated by two base pairs so that the two tomaymycin-modified guanines are now only four base-pairs apart, the two species of tomaymycin mols. are still bound with the same stereochem. and orientation, and the 10-mer duplex adduct maintains its self-complementarity. In a second 10-mer duplex it was shown that changing the bonding sequence from 5'CGA to 5'AGC does not significantly affect the structure of the bis-tomaymycin-duplex adduct. However, when the sequence is rearranged so that the drugs point in a tail-to-tail orientation rather than in the previous head-to-head configuration, there are more than one species of tomaymycin bound to DNA, and, as a consequence, the bis-tomaymycin 10-mer duplex adduct loses its self-complementarity. The 10-mer duplex contg. the 5'CGA sequence, in which the tomaymycin mols. are oriented head to head was used to design an interstrand crosslinking species in which the two drug mols. are linked together with a flexible linker mol.
IT **140676-21-7**
RL: BIOL (Biological study)
(as DNA-DNA interstand crosslinker, design of, tomaymycin-deoxyoligonucleotide adduct in relation to)
RN 140676-21-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



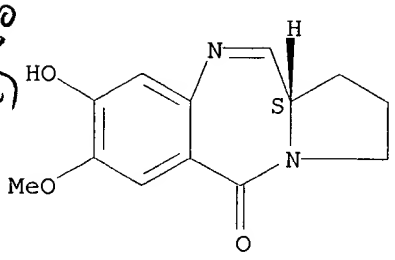
L16 ANSWER 54 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1992:255585 CAPLUS
DN 116:255585
TI Rational design of a highly efficient irreversible DNA interstrand cross-linking agent based on the pyrrolobenzodiazepine ring system
AU Bose, D. Subhas; Thompson, Andrew S.; Ching, Jingshan; Hartley, John A.; Berardini, Mark D.; Jenkins, Terence C.; Neidle, Stephen; Hurley, Laurence H.; Thurston, David E.
CS Sch. Pharm. Biomed. Sci., Portsmouth Polytech., Portsmouth, PO1 2DZ, UK
SO J. Am. Chem. Soc. (1992), 114(12), 4939-41
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
GI



I

AB Pyrrolo[2,1-c][1,4]benzodiazepine C8 dimer DSB-120 (I) was prepd. and its DNA binding studied. I is a remarkably efficient crosslinking agent, showing activity down to at least 0.01 .mu.M and >90% crosslinking at 0.4 .mu.M. Extensive modeling studies of I with d(CGYGXXCYCG)2 show that the spatial sepn. of the pyrrolobenzodiazepine units is optimal for spanning 6 base pairs with a preference for 5'-PuGATCPy or 5'-PyGATCPu sequences, and that it actively recognizes the embedded d(GTAC)2 sequence. 1H NMR of the 1:1 adduct of I and the self-complementary 10-mer d(CICGATCICG)2 showed that the duplex is crosslinked sym. via the minor groove N2 positions of the guanines, with 11S,11S' stereochem. in the ligand, and minor distortion of the helix.
IT **81307-24-6**, Antibiotic DC 81
RL: RCT (Reactant)
(antitumor and DNA binding activities of)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



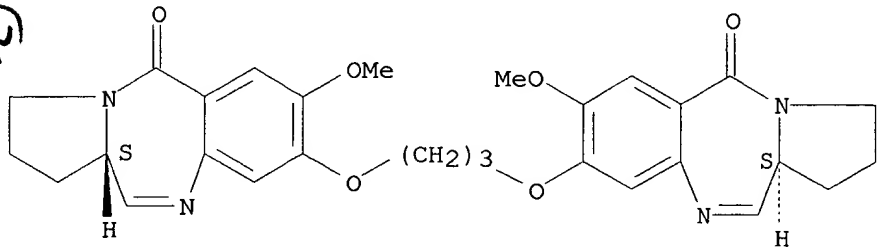
IT **140676-21-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., antitumor, and DNA binding activities of)

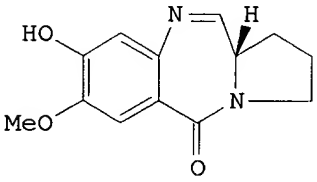
RN 140676-21-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

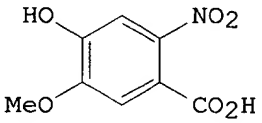
Absolute stereochemistry.



L26 ANSWER 55 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1992:193997 CAPLUS
DN 116:193997
TI New approaches to pyrrolo[2,1-c][1,4]benzodiazepines: synthesis, DNA-binding and cytotoxicity of DC-81
AU Rose, D. Subhas; Jones, Gary B.; Thurston, David E.
CS Sch. Pharm. Biomed. Sci., Portsmouth Polytech., Portsmouth/Hants., PO1 2DZ, UK
SO Tetrahedron (1992), 48(4), 751-8
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
OS CASREACT 116:193997
GI



I

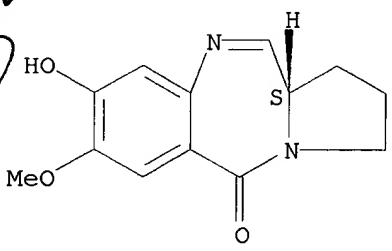


II

AB Two routes to the naturally occurring DNA-binding antitumor antibiotic DC-81 (I) are described, one of which involves a novel cyclization process based on acid resin. The second route involves the synthesis of a new compd., 6-nitrovanillic acid (II), a key A-ring component of many naturally occurring title compds. These routes have provided a sufficient quantity of DC-81 to allow complete characterization and evaluation in DNA-binding and in vitro cytotoxicity studies.

IT **81307-24-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., DNA-binding and cytotoxicity of)
RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

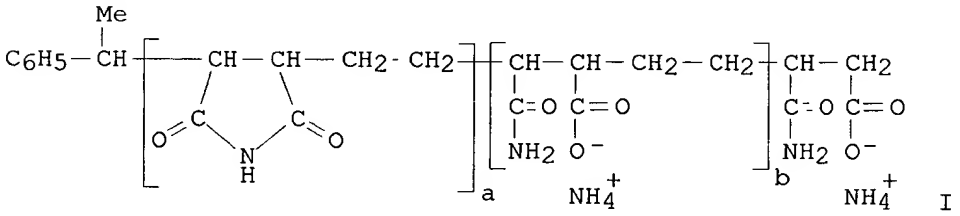
Absolute stereochemistry.



L26 ANSWER 56 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1992:99301 CAPLUS
DN 116:99301
TI Maleic anhydride copolymers as antidotes for the cytotoxicity of neoplasm inhibitors
IN Bach, Ardalan; Shanahan, William R., Jr.
PA Searle, G. D., and Co., USA
SO Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 393575	A1	19901024	EP 1990-107246	19900417
	EP 393575	B1	19940316		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2014732	AA	19901017	CA 1990-2014732	19900417
	JP 02292227	A2	19901203	JP 1990-101530	19900417
	AT 102838	E	19940415	AT 1990-107246	19900417
	ES 2062155	T3	19941216	ES 1990-107246	19900417
PRAI	US 1989-339503		19890417		
	EP 1990-107246		19900417		

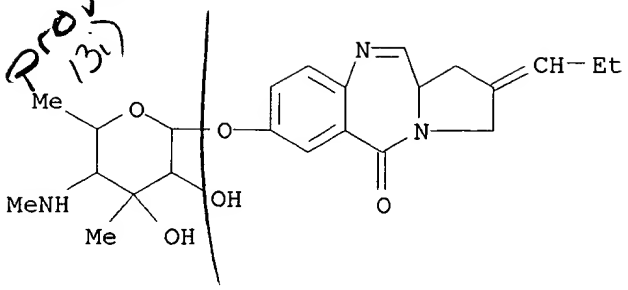
OS MARPAT 116:99301
GI



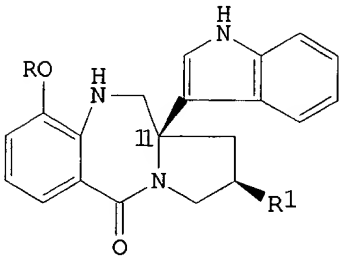
I

AB Half-amide:half-imide copolymers comprising ethylene and maleic anhydride moieties (structure given), specifically carbetimer (I; a/b = 1:2-5), decrease the cytotoxic side effects of neoplasm inhibitors. Mice treated i.v. with 21 mg adriamycin/kg died within 5 days. When 1700 mg I/kg was administered concomitantly, no lethality was shown for >30 days.
IT **117782-84-0**, Sibanomicin
RL: PRP (Properties)
(cytotoxicity of, maleic anhydride copolymer antidote for)
RN 117782-84-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-propylidene-, (2E)- (9CI) (CA INDEX NAME)

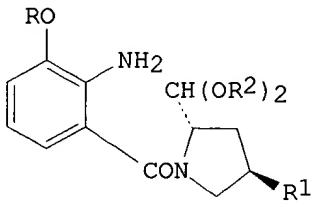
Proviso (13)



L26 ANSWER 57 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1991:535788 CAPLUS
DN 115:135788
TI New methods and reagents in organic synthesis. 92. A stereoselective synthesis of tilivalline and its analogs
AU Mori, Shigehiro; Ohno, Tomoyasu; Harada, Hiroshi; Aoyama, Toyohiko; Shioiri, Takayuki
CS Fac. Pharm. Sci., Nagoya City Univ., Nagoya, 467, Japan
SO Tetrahedron (1991), 47(27), 5051-70
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
OS CASREACT 115:135788
GI



I

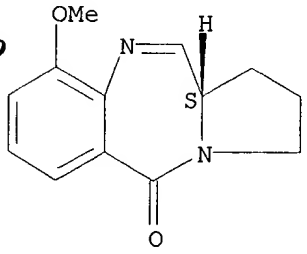


II

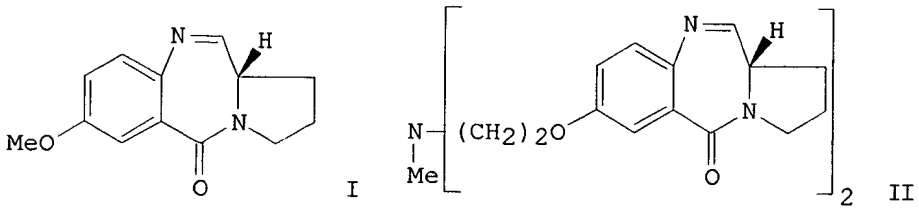
AB Tilivalline I (R = R1 = H) and its derivs. I (R = H, Me, PhCH2; R1 = H, HO, PhCH2O) were efficiently and stereoselectively prepd. The key step was the one-pot intramol. cyclocondensation of aminobenzoylpyrrolidinecarboxamides II (R2 = Me, Et) and stereoselective addn. of indole. The use of different nucleophiles gave a series of 11-substituted 5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-ones.

IT **110715-89-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and addn. reaction of, with indole)
RN 110715-89-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 58 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1991:239940 CAPLUS
DN 114:239940
TI DNA binding properties of a new class of linked anthramycin analogs
AU Farmer, J. Dean, Jr.; Gustafson, Gary R.; Conti, Andrea; Zimm, Matthew B.; Suggs, J. William
CS Dep. Chem., Brown Univ., Providence, RI, 02912, USA
SO Nucleic Acids Res. (1991), 19(4), 899-904
CODEN: NARHAD; ISSN: 0305-1048
DT Journal
LA English
GI



I II

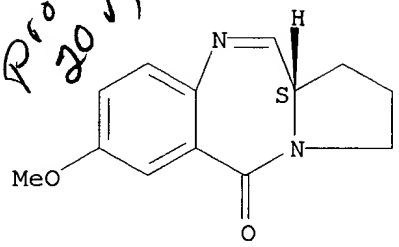
AB The DNA-binding properties of the anthramycin analogs I, II, and III were studied using fluorescence spectroscopy. A considerable fluorescence enhancement occurs when pyrrolo[1,4]benzodiazepines (P[1,4]Bs) are covalently attached to duplex DNA, which was used to show that neither the presence of RNA, single-stranded DNA, or protein had any effect on the degree of fluorescence enhancement resulting from the incubation of II and III with DNA. The enhancement was found to be dependent on the presence of the imine functionality in each of the compds. A wavelength of 320 nm was used to excite the chromophore and its emission wavelength max. was 420 nm. Addnl., it was discovered that the P[1,4]B ring system exhibits exceptionally favorable fluorescence polarization anisotropy (FPA) decay characteristics. For these more detailed fluorescence measurements, the structurally simpler analog I was used. The time-resolved max. FPA for I in glycerol at 25.degree. is 0.28. This result indicates that the P[1,4]B family of antibiotics could serve as sensitive probes of DNA dynamics in the 0.1 to 35 ns time scale.

IT **133954-34-4 133954-35-5 133954-36-6**
RL: BIOL (Biological study)
(binding of, to DNA, characterization of)

RN 133954-34-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

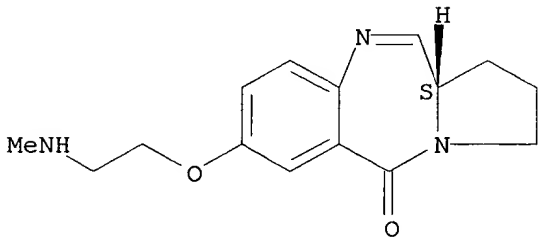
Absolute stereochemistry.

Proviso 20 J



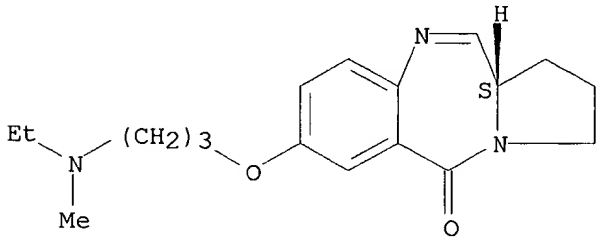
RN 133954-35-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-[2-(methylamino)ethoxy]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

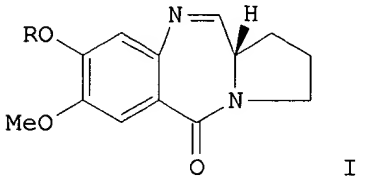


RN 133954-36-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[3-(ethylmethylamino)propoxy]-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 59 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1990:423460 CAPLUS
DN 113:23460
TI O-Debenzylation of a pyrrolo[2,1-c][1,4]benzodiazepine in the presence of a carbinolamine functionality: synthesis of DC-81
AU Thurston, David E.; Murty, Varanasi S.; Langley, David R.; Jones, Gary B.
CS Sch. Pharm., Portsmouth Polytech., Hants, PO1 2DZ, UK
SO Synthesis (1990), (1), 81-4
CODEN: SYNTBF; ISSN: 0039-7881
DT Journal
LA English
OS CASREACT 113:23460
GI

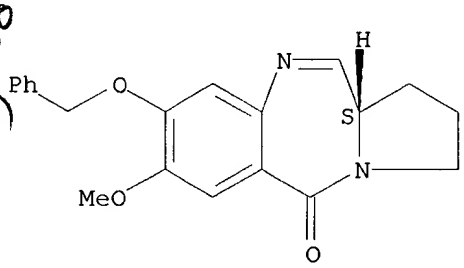


I

AB In contrast to other methods of redn., catalytic transfer hydrogenation allows debenzylation of a phenolic hydroxyl in a carbinolamine-contg. pyrrolo[2,1-c][1,4]benzodiazepine, while leaving the biol.-important carbinolamine moiety intact. This has been demonstrated by synthesis of DC-81 (I, R = H) from 3,4-MeO(HO)C6H3CO2H via 4-benzyloxy-5-methoxy-2-nitrobenzoic acid and I (R = CH2Ph).

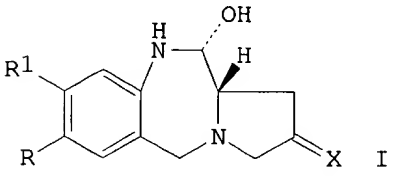
IT **127810-79-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and debenzylation of, by mercuric chloride-calcium carbonate)
RN 127810-79-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **89824-22-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 89824-22-6 CAPLUS

L26 ANSWER 60 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1989:632415 CAPLUS
DN 111:232415
TI Photochemical approach to the synthesis of the pyrrolo[1,4]benzodiazepine antibiotics
AU Weidner-Wells, Michele A.; DeCamp, Ann; Mazzocchi, Paul H.
CS Dep. Chem. Biochem., Univ. Maryland, College Park, MD, 20742, USA
SO J. Org. Chem. (1989), 54(24), 5746-58
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
OS CASREACT 111:232415
GI

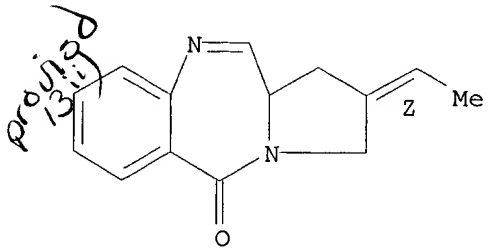


I

AB The total syntheses of the pyrrolo[1,4]benzodiazepine antitumor antibiotics prothracarcin I (X = CHMe, R = R1 = H), and DC-81 I (X = H2, R = OMe, R1 = OH) were realized using, as a key step, the photochem. [2.sigma. + 2.pi.] ring expansion of the appropriately substituted N-pentenylphthalimide to afford the corresponding pyrrolobenzazepinedione. Conversion of the photoproduct into the antibiotic skeleton was effected by transformation of the benzylic ketone into a carbinolamine via a Curtius rearrangement sequence.

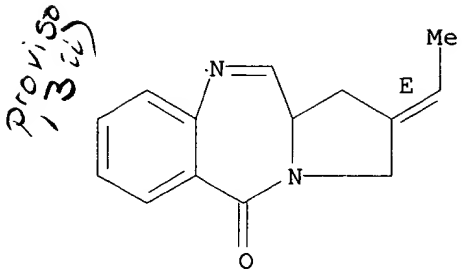
IT **123355-35-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 123355-35-1 CAPLUS
IT **105498-28-0P 105498-29-1P 123355-42-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of)
RN 105498-28-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

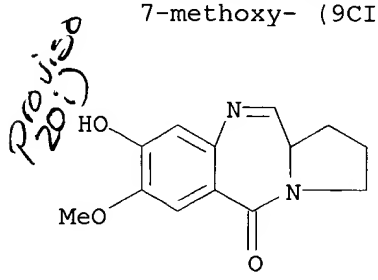


RN 105498-29-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



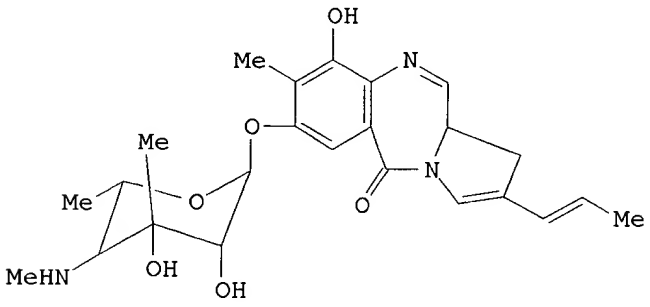
RN 123355-42-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy- (9CI) (CA INDEX NAME)



L26 ANSWER 61 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1989:630672 CAPLUS
DN 111:230672
TI Novel anticancer antibiotic DC-105 and its manufacture with Streptomyces
IN Nakano, Hirofumi; Takahashi, Isami; Asano, Kozo; Koda, Mayumi; Ashizawa, Tadashi
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 01121296	A2	19890512	JP 1987-277696	19871102

GI

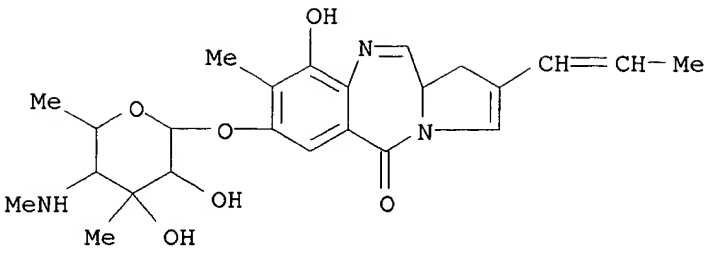


I

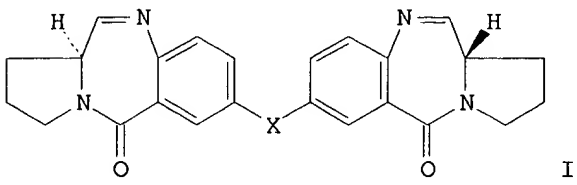
AB Anticancer antibiotic DC-105 (I) is manufd. by cultivation of I-producing Streptomyces. The culture medium was filtered, and the filtrate (100 L) was subjected to a series of chromatog. columns to produce 28 mg I, which at 0.03 mg/kg i.p. showed 128% T/C (treated group/control group) survival time in lymphocytic leukemia P-388-bearing mice, vs. 151%, for mitomycin C at 6 mg/kg. Streptomyces DO-105 was shake-cultured in a medium contg. tryptone, yeast ext., meat ext., hydrolyzable starch, glucose, and CaCO3; then aerobically shake-cultured in a medium contg. dextrin, soybean powder, and salts at 28.degree. for 70 h. An injection soln. was formulated contg. 10 mg I and .apprx.10 mL physiol. saline soln.

IT **123731-93-1P**, Antibiotic DC 105
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manuf. of, with Streptomyces DO-105, anticancer activity of)

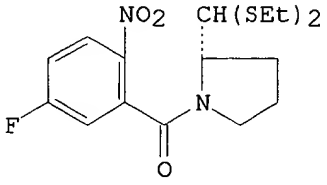
RN 123731-93-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,11a-dihydro-9-hydroxy-8-methyl-2-(1-propenyl)- (9CI) (CA INDEX NAME)


OH
Me
N
CH═ CH— Me
Me
O
O
N
MeNH
OH
O
Me
OH

L26 ANSWER 62 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1989:573848 CAPLUS
DN 111:173848
TI Synthesis and DNA crosslinking ability of a dimeric anthramycin analog
AU Farmer, J. Dean, Jr.; Rudnicki, Suzanne M.; Suggs, J. William
CS Dep. Chem., Brown Univ., Providence, RI, 02912, USA
SO Tetrahedron Lett. (1988), 29(40), 5105-8
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 111:173848
GI



I



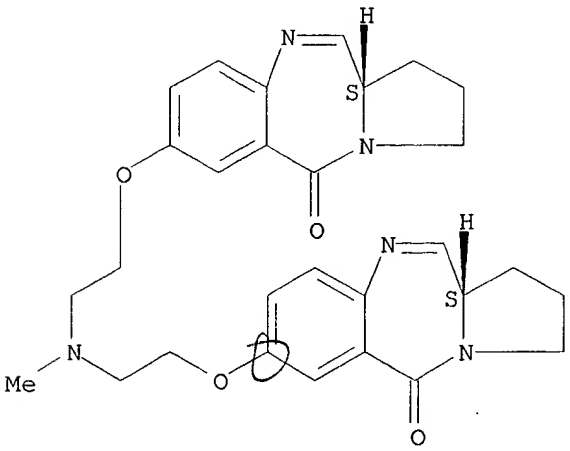
II

AB Linked analogs I [X = S(CH2)6S, OCH2CH2NMeCH2CH2O] of the DNA binding antibiotic anthramycin are made via nucleophilic arom. substitution of benzoylpyrrolidinecarboxaldehyde deriv. II followed by redn.-cyclization. The linked compds. protect DNA from restriction endonucleases and reversibly crosslink DNA.

IT **123064-64-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and DNA crosslinking by)

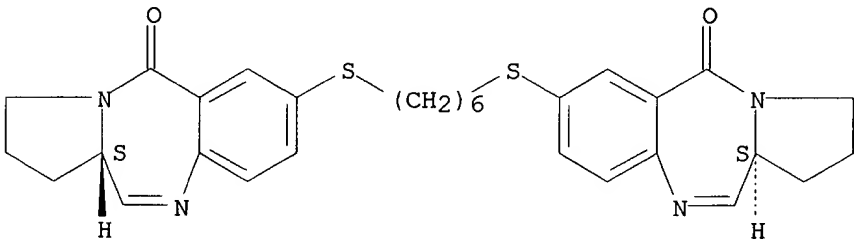
RN 123064-64-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,7'-[(methylimino)bis(2,1-ethanediyloxy)]bis[1,2,3,11a-tetrahydro-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **123064-63-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 123064-63-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,7'-[1,6-hexanediylbis(thio)]bis[1,2,3,11a-tetrahydro-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

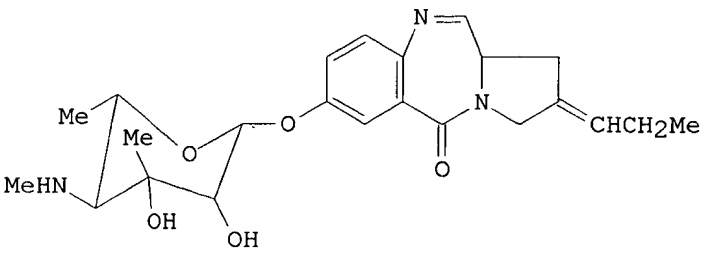
Absolute stereochemistry.



L26 ANSWER 63 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1989:93559 CAPLUS
DN 110:93559
TI Antitumor antibiotic SF 2364 and its manufacture with Micromonospora
IN Ito, Jiro; Watabe, Hiromi; Ishii, Narutaka; Gomi, Shuichi; Nagasawa, Mieko; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi
PA Meiji Seika Kaisha, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 63107992	A2	19880512	JP 1986-251887	19861024

GI

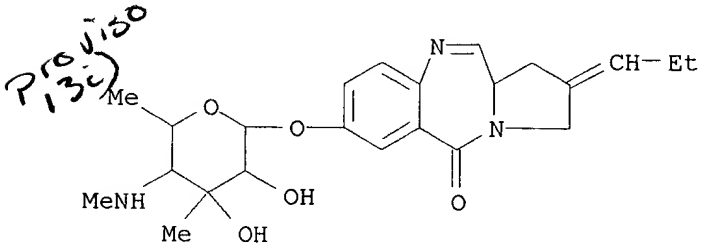


I

AB Antitumor antibiotic SF2364 (I) is manufd. by cultivating Micromonospora. Micromonospora was cultivated in a 200-L prodn. medium contg. sucrose, wheat germ, salts, etc. at 28.degree. for 3 days with aeration and agitation. The culture filtrate was chromatographed to obtain I.HCl 500 mg.

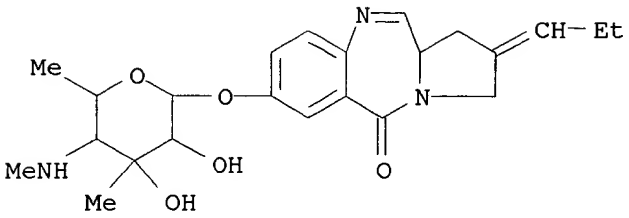
IT **117782-84-0DP**, salts **117782-84-0P 119180-42-6P**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manuf. of, with Micromonospora)

RN 117782-84-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-propylidene-, (2E)- (9CI) (CA INDEX NAME)

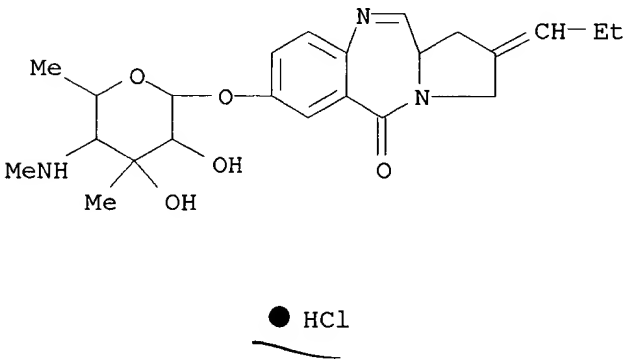


RN 117782-84-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-

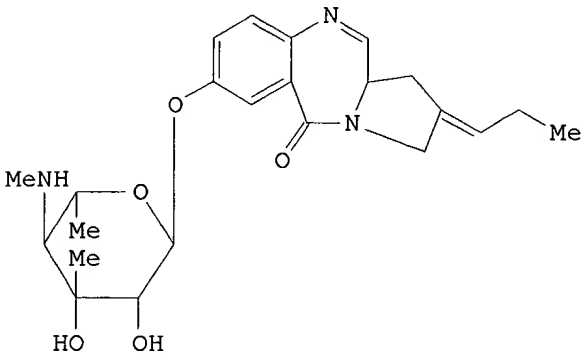
propylidene-, (2E)- (9CI) (CA INDEX NAME)



RN 119180-42-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-propylidene-, monohydrochloride (9CI) (CA INDEX NAME)



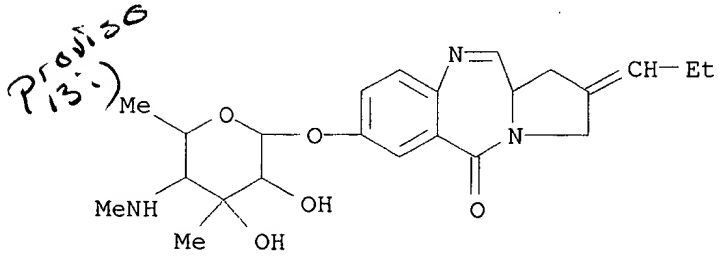
L26 ANSWER 64 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1989:4230 CAPLUS
DN 110:4230
TI Sibanomicin, a new pyrrolo[1,4]-benzodiazepine antitumor antibiotic produced by a Micromonospora sp
AU Itoh, Jiro; Watabe, Hiroomi; Ishii, Shigetaka; Gomi, Shuichi; Nagasawa, Mieko; Yamamoto, Haruo; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi
CS Pharm. Res. Lab., Meiji Seika Kaisha, Ltd., Yokohama, 222, Japan
SO J. Antibiot. (1988), 41(9), 1281-4
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI



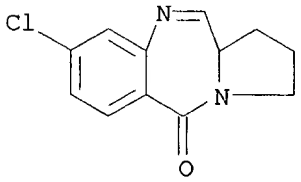
I

AB The prodn., isolation, characterization, structural elucidation, and biol. properties of a new antibiotic from Micromonospora sp. SF 2364, sibanomycin (I), are reported. The UV spectra of I indicated that it belongs to the anthramycin group. The mol. formula for the hydrochloride of I was C23H31O5.HCl. Whereas the antimicrobial activity of I was very weak, it did show a marked prolongation of the life in mice bearing leukemia P388 cells.

IT **117782-84-0**
RL: BIOL (Biological study)
(antitumor antibiotic, from Micromonospora)
RN 117782-84-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-propylidene-, (2E)- (9CI) (CA INDEX NAME)

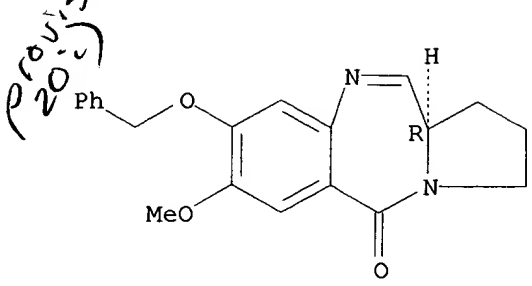


L26 ANSWER 65 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1988:621909 CAPLUS
DN 109:221909
TI Pyrrolo[1,4]benzodiazepine antitumor antibiotics: relationship of DNA alkylation and sequence specificity to the biological activity of natural and synthetic compounds
AU Hurley, Laurence H.; Reck, Teri; Thurston, David E.; Langley, David R.; Holden, Kenneth G.; Hertzberg, Robert P.; Hoover, John R. E.; Gallagher, Gregory, Jr.; Faucette, Leo F.; et al.
CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA
SO Chem. Res. Toxicol. (1988), 1(5), 258-68
CODEN: CRTOEC
DT Journal
LA English
AB The DNA alkylation and sequence specificity of a group of natural and synthetic pyrrolo[1,4]benzodiazepines [P(1,4)Bs] were evaluated by using an exonuclease III stop assay, and the results were compared with in vitro and in vivo biol. potency and antitumor activity. The P(1,4)B antibiotics are potent antitumor agents produced by various Actinomycetes, which are believed to mediate their cytotoxic effects by covalent bonding through N-2 of guanine in the minor groove of DNA. The results of a sensitive DNA alkylation assay using exonuclease III that permits both estn. of the extent of DNA modification as well as location of the precise guanines to which the drugs are covalently bound are described. Using this assay, a series of natural and synthetic compds. of the P(1,4)B class was evaluated for their ability to bond to DNA; also their DNA sequence preference was detd. The compds. included are P(1,4)Bs carrying different substituents in the arom. ring, having varying degrees of satn. in the 5-membered ring, or differing in the stereochem. at C-11a. These same compds. were evaluated for in vitro cytotoxic activity against B16 melanoma cells, for potency in vivo in B6D2F1 mice (LD50), and for antitumor activity (ILSmax) against P388 leukemia cells. A good correlation was found between extent of DNA bonding and in vitro and in vivo potency. Furthermore, on the basis of electronic and steric considerations, it was possible to rationalize why those compds. that showed negligible biol. activity were unable to bond covalently to DNA. The degree of satn. in the five-membered ring of the P(1,4)Bs had a significant effect on the DNA bonding reactivity and biol. activity of this class of compds.
IT **116564-84-2P 116564-97-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 116564-84-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8-chloro-1,2,3,11a-tetrahydro- (9CI) (CA INDEX NAME)



RN 116564-97-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

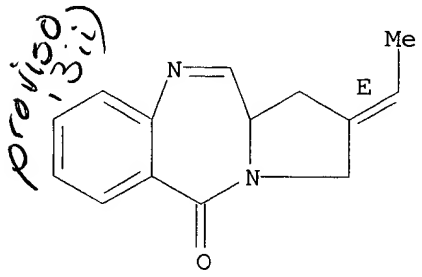


L26 ANSWER 66 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1988:492593 CAPLUS
DN 109:92593
TI The total synthesis of DC-81, a pyrrolo[1,4]benzodiazepine antitumor antibiotic
AU Weidner, Michele Ann
CS Univ. Maryland, College Park, MD, USA
SO (1987) 245 pp. Avail.: Univ. Microfilms Int., Order No. DA8725588
From: Diss. Abstr. Int. B 1988, 48(8), 2328-9
DT Dissertation
LA English
AB Unavailable
IT **89824-22-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of)
RN 89824-22-6 CAPLUS

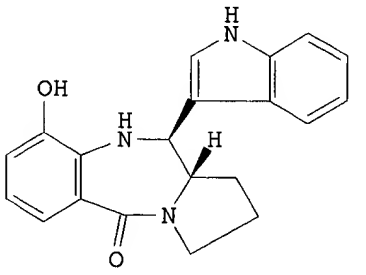
proviso 20

L26 ANSWER 67 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1987:598720 CAPLUS
DN 107:198720
TI New synthesis of heterocycles by use of organometallic complexes: the application to the syntheses of biologically active substances
AU Mori, Miwako
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan
SO Yakugaku Kenkyu no Shinpo (1986), 2, 127-50
CODEN: YAKSEY
DT Journal
LA Japanese
AB A symposium on the formation of 1,4-benzodiazepine skeleton from o-haloanilines and amino acids via palladium catalyzed carbonylation. The total syntheses of anthramycin, prothracarcin, tomaymycin, SEN-215, and neothramycin, which were antitumor antibiotics were achieved in good overall yields from 1-proline or 4-hydoxy-1-proline as amino acid. A one step synthesis of quinazolines from o-haloanilines and five membered lactams or primary amines was developed by use of palladium catalyzed carbonylation. Though the alkylmetal complex could not be synthesized from the alkyl halide, .alpha.-halocarbonyl compds. such as .alpha.-halo amides, .alpha.-halo esters, .alpha.-halo ketones, and .alpha.-halo nitriles having internal double bonds were treated with Pd(PPh3)4 to afford the cyclized products in good yields presumably through the .sigma.-alkylmetal complex. By use of this method, pyrrolizidine alkaloids and oxacepham skeleton were synthesized.
IT **105498-29-1P**, (.+-.)-Prothracarcin
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of)
RN 105498-29-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (E)- (9CI) (CA INDEX NAME)

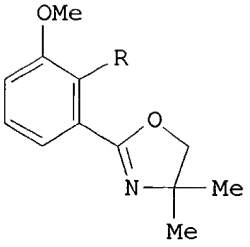
Double bond geometry as shown.



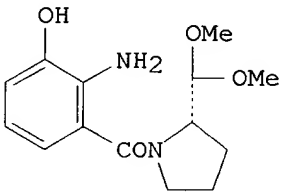
L26 ANSWER 68 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1987:575731 CAPLUS
DN 107:175731
TI Stereoselective total synthesis of tilivalline
AU Mori, Shigehiro; Aoyama, Toyohiko; Shioiri, Takayuki
CS Fac. Pharm. Sci., Nagoya City Univ., Japan
SO Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1986), 28th, 481-7
CODEN: TYKYDS
DT Journal
LA Japanese
GI



I



II



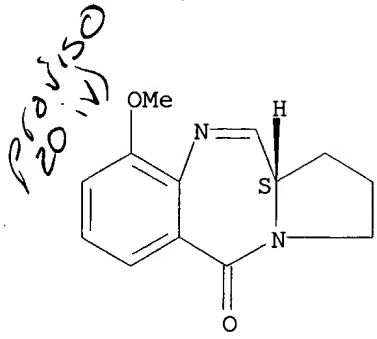
IV

AB Stereoselective synthesis of tilivalline (I) is described. Oxozoline II (R = H) was aminated to give II (R = NH2) which was hydrolyzed with HCl in the presence of red P to give m-hydroxyanthranilic acid (III). Condensation of III with L-prolinal dimethylacetal hydrochloride by the (EtO)2P(O)CN afforded the amide IV. Successive treatment of IV with Me3SiCl, and NaI in pyridine, followed by indole, and ZnCl2 in a one-pot process gave I in excellent yield.

IT **110715-89-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 110715-89-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.


OMe
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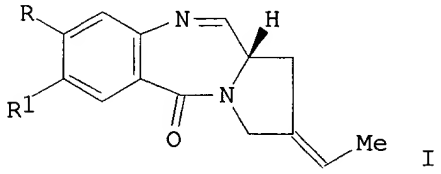
L26 ANSWER 69 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1987:458707 CAPLUS
DN 107:58707
TI Total syntheses of prothracarcin and tomaymycin by use of palladium catalyzed carbonylation
AU Mori, Miwako; Uozumi, Yasuhiro; Kimura, Masaya; Ban, Yoshio
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan
SO Tetrahedron (1986), 42(14), 3793-806
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
OS CASREACT 107:58707
GI

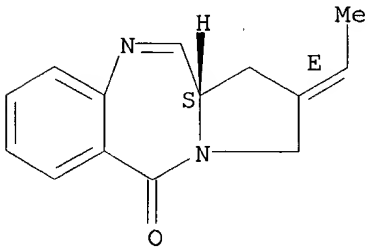


I

AB Total synthesis of optically active prothracarcin (I, R = R1 = H) and pretomaymycin (I, R = OH, R1 = OMe), which is readily convertible to tomaymycin, were achieved via a Pd-catalyzed carbonylation. The structure of prothracarcin was detd. to be (11aS)(E)-I (R = R1 = H) by comparison of the 13C-NMR spectra of the synthetic E- and Z-isomers.

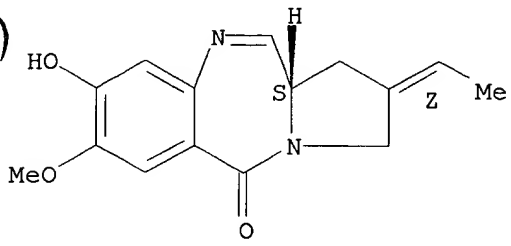
IT **81542-99-6P**, Prothracarcin
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mol. structure of)
RN 81542-99-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



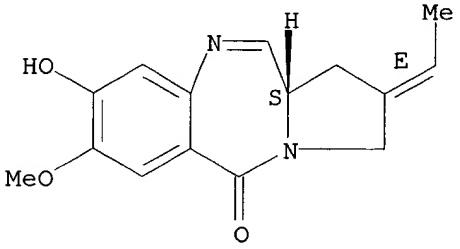
IT **81422-29-9P 81422-30-2P**, Pretomaymycin
105120-29-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 81422-29-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



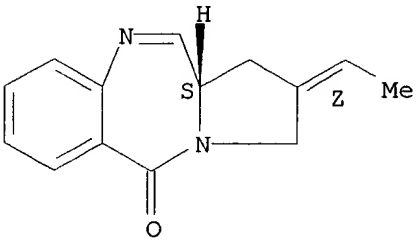
RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

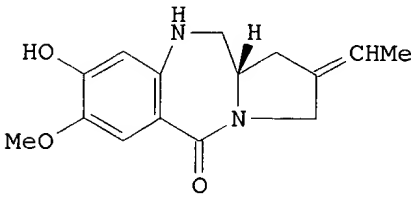


RN 105120-29-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L26 ANSWER 70 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1987:84241 CAPLUS
DN 106:84241
TI Structure and syntheses of SEN-215 and oxotomaymycin
AU Mori, Miwako; Uozumi, Yasuhiro; Ban, Yoshio
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan
SO Heterocycles (1986), 24(5), 1257-60
CODEN: HTCYAM; ISSN: 0385-5414
DT Journal
LA English
OS CASREACT 106:84241
GI



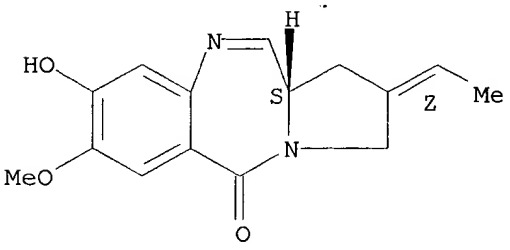
I

AB The structure of SEN-215 was detd. as (11aS)(E)-2-ethylidene-2,3,5,10,11,11a-hexahydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepine (I) by conversion of (E)- and (Z)-pretomaymycin into (E)- and (Z)-I.

IT **81422-29-9P 81422-30-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)

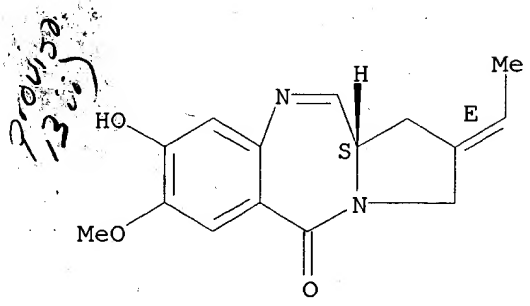
RN 81422-29-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

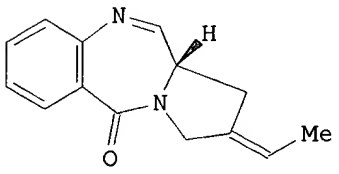


RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.


Me
H
N
E
HO
S
N
MeO
O

L26 ANSWER 71 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1987:66984 CAPLUS
DN 106:66984
TI A versatile and efficient synthesis of carbinolamine-containing pyrrolo[1,4]benzodiazepines via the cyclization of N-(2-aminobenzoyl)pyrrolidine-2-carboxaldehyde diethyl thioacetals: total synthesis of prothracarcin
AU Langley, David R.; Thurston, David E.
CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA
SO J. Org. Chem. (1987), 52(1), 91-7
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
OS CASREACT 106:66984
GI

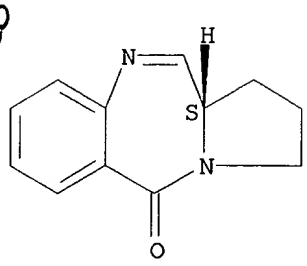


I

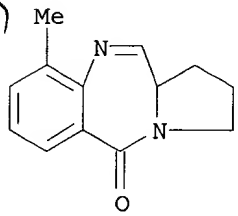
AB A versatile and efficient synthesis of carbinolamine-contg. pyrrolo[1,4]benzodiazepines (or the corresponding imine forms) is described that involves HgCl2-mediated cyclization of the corresponding N-(2-aminobenzoyl)pyrrolidine-2-carboxaldehyde di-Et thioacetals. This new synthesis has significant advantages over previously existing methods in that (a) catalytic hydrogenation is not involved in the cyclization process, thus allowing preservation of unsatn. in the product, (b) all steps are mild and take place in high yields, (c) the success of the reaction is apparently independent of substituent effects, (d) the reaction proceeds with retention of stereochem. at the aldehyde bearing carbon, and (e) it can be readily adapted for the convergent synthesis of a variety of analogs. In addn. to the synthesis of some model carbinolamine-contg. compds., the overall utility of this procedure is demonstrated by the total synthesis of prothracarcin (I), a natural product with antitumor activity from Streptomyces umbrosus. This allowed confirmation of the E configuration previously assigned to the C2-ethylidene side chain of I.

IT **72435-89-3P 100231-11-6P 100231-12-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

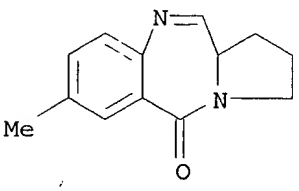
Absolute stereochemistry. Rotation (+).



RN 100231-11-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methyl- (9CI) (CA INDEX NAME)

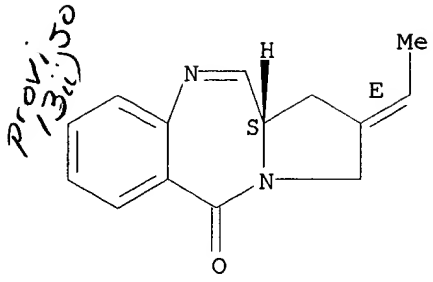


RN 100231-12-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



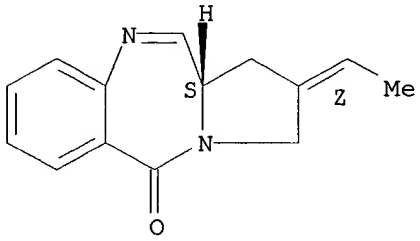
IT **81542-99-6P**, Prothracarcin **105120-29-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of)
RN 81542-99-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



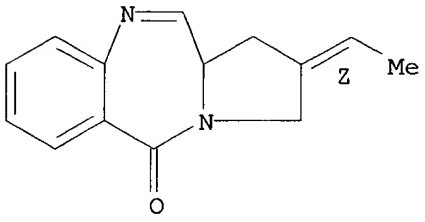
RN 105120-29-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



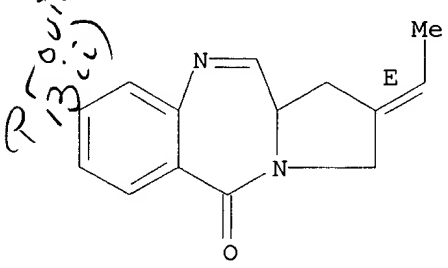
L26 ANSWER 72 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1986:627189 CAPLUS
DN 105:227189
TI Part I. The total synthesis of the pyrrolo(1,4)benzodiazepines E and Z-prothracarcin. Part II. Carbohydrate-based approaches to the C33-37 portion of amphotericin B
AU Schuda, Ann DeCamp
CS Univ. Maryland, College Park, MD, USA
SO (1985) 238 pp. Avail.: Univ. Microfilms Int., Order No. DA8604216 From: Diss. Abstr. Int. B 1986, 46(12), Pt. 1, 4249-50
DT Dissertation
LA English
AB Unavailable
IT **105498-28-0P 105498-29-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of)
RN 105498-28-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

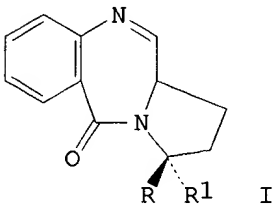


RN 105498-29-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L26 ANSWER 73 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1986:572417 CAPLUS
DN 105:172417
TI A one step synthesis of 1,4-benzodiazepines: synthetic studies on neothramycin
AU Mori, Miwako; Kimura, Masaya; Uozumi, Yasuhiro; Ban, Yoshio
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan
SO Tetrahedron Lett. (1985), 26(48), 5947-50
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 105:172417
GI

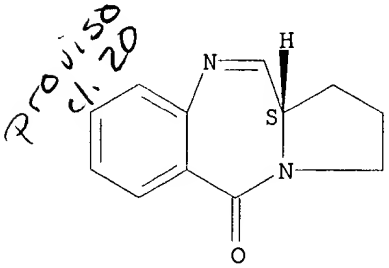


I

AB A one step synthesis of 1,4-benzodiazepines from o-haloanilines and amino acids was achieved by use of palladium catalyzed carbonylation, by which application a synthesis of the model compds. I (R = MeO, R1 = H; R = H; R1 = MeO) of Neothramycin (A and B) was described. An efficient chemoselective redn. of the amide was provided.

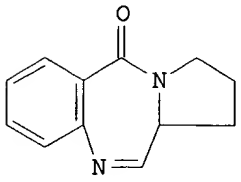
IT **72435-89-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

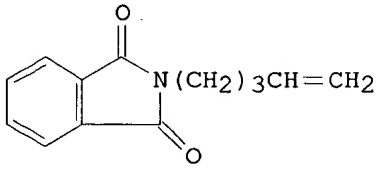
Absolute stereochemistry. Rotation (+).

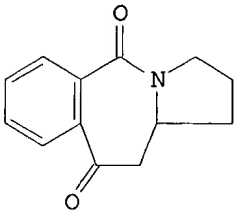


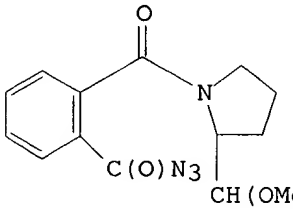
Proviso cl. 20

L26 ANSWER 74 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1986:406496 CAPLUS
DN 105:6496
TI A photochemical route to pyrrolo[1,4]benzodiazepine antitumor antibiotics
AU Mazzocchi, Paul H.; Schuda, Ann DeCamp
CS Dep. Chem., Univ. Maryland, College Park, MD, 20742, USA
SO Heterocycles (1985), 23(7), 1603-6
CODEN: HTCYAM; ISSN: 0385-5414
DT Journal
LA English
OS CASREACT 105:6496
GI


I


II


III

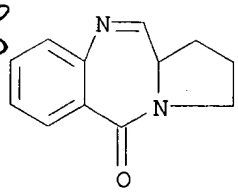

IV

AB The ketone I, contg. the title ring system, was prepd. in a sequence involving the photochem. ring expansion of the phthalimide II to the dioxopyrrolobenzazepine III and a Curtius rearrangement of a ring opened III derived compd. IV.

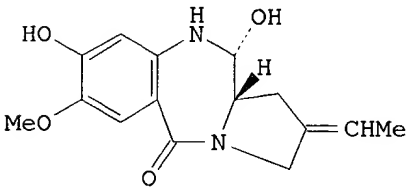
IT **102609-85-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 102609-85-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro- (9CI) (CA INDEX NAME)



L26 ANSWER 75 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1986:199669 CAPLUS
DN 104:199669
TI Pyrrolo[1,4]benzodiazepine antitumor antibiotics: evidence for two forms of tomaymycin bound to DNA
AU Barkley, Mary D.; Cheatham, Steve; Thurston, David E.; Hurley, Laurence H.
CS Med. Cent., Univ. Kentucky, Lexington, KY, 40536, USA
SO Biochemistry (1986), 25(10), 3021-31
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
GI

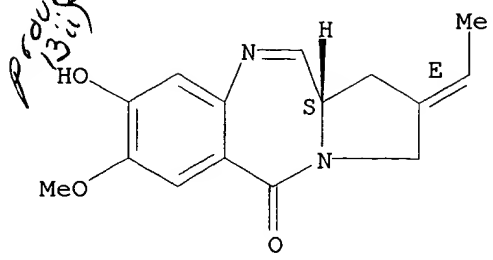


I

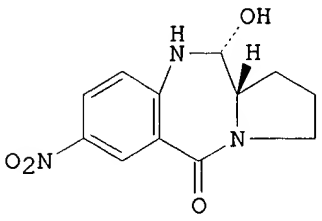
AB Two fluorescent ground-state species of tomaymycin (I), an antibiotic belonging to the pyrrolo[1,4]benzodiazepine group of antitumor compds., were obsd. in protic solvents and in its adducts with DNA; 1H NMR studies showed that the 2 fluorescent species in MeOH were the 11R,11aS-[35050-55-6] and 11S,11aS-11-Me ether of tomaymycin [101313-08-0]. On the basis of epimerization expts. and exchange of 13C from 13MeOH into the C-11 methoxy group of the tomaymycin Me ether, a mechanism is proposed for their interconversion via 10,11-anhydrotomaymycin [**81422-30-2**]. Coupling information revealed that the soln. conformations of the 2 diastereomers differ, with the C-5 carbonyl lying closer to the plane of the arom. ring in the 11R,11aS diastereomer. The fluorescence excitation and emission spectra of the 2 emitting species in MeOH were sepd. by time-resolved fluorescence spectroscopy and were assocd. with the diastereomeric forms identified by 1H NMR. Time-resolved fluorescence studies of tomaymycin in protic solvents and on DNA indicated that the absorption spectrum of the longer lifetime component (11R,11aS form) is red-shifted relative to the absorption spectrum of the shorter lifetime component (11S,11aS form), consistent with more extensive conjugation. The 2 conformational forms of tomaymycin on DNA were tentatively identified as the 11S,11aS and 11R,11aS diastereomeric adducts, which bind in opposite orientations in the minor groove. This proposal is supported by mol. modeling studies with the use of a hexamer adduct of d(ATGCAT)2.

IT **81422-30-2**
RL: BIOL (Biological study)
(tomaymycin Me ether epimerization mechanism in relation to)
RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.


HO
MeO
N
H
S
N
O
E
Me

L26 ANSWER 76 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1986:168234 CAPLUS
DN 104:168234
TI Synthesis and structure of anthramycin analogs via hydride reduction of dilactams
AU Suggs, J. William; Wang, Yueh Sha; Lee, Ken S.
CS Dep. Chem., Brown Univ., Providence, RI, 02912, USA
SO Tetrahedron Lett. (1985), 26(40), 4871-4
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 104:168234
GI



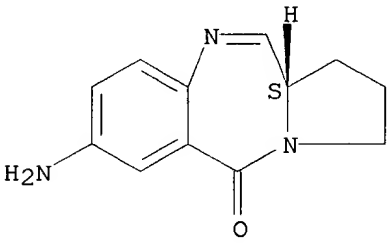
I

AB Hydride redn. of pyrrolo[1,4]benzodiazepin-5,10-diones to carbinolamines is possible if a sufficiently electron-withdrawing group, such as NO2, is present on the arom. ring. The x-ray structure of one such product, I, is given.

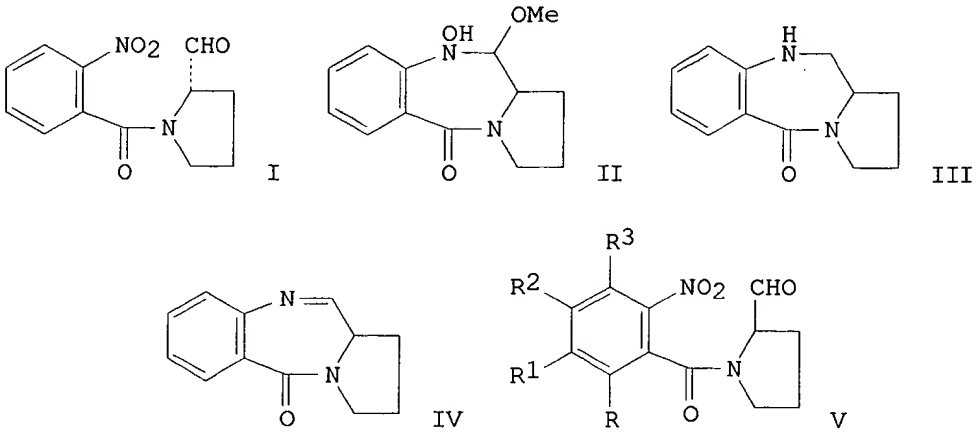
IT **101664-41-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and quaternization of)

RN 101664-41-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-amino-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



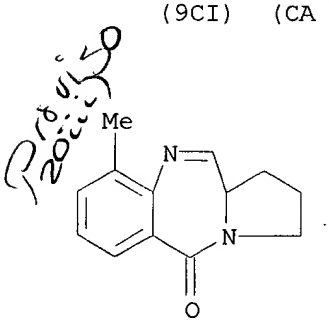
L26 ANSWER 77 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1986:129877 CAPLUS
DN 104:129877
TI Synthesis and stereochemistry of carbinolamine-containing pyrrolo[1,4]benzodiazepines by reductive cyclization of N-(2-nitrobenzoyl)pyrrolidine-2-carboxaldehydes
AU Thurston, David E.; Langley, David R.
CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA
SO J. Org. Chem. (1986), 51(5), 705-12
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
OS CASREACT 104:129877
GI



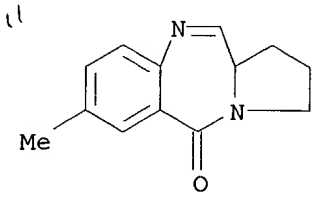
AB Products from the reductive cyclization (H, Pd/C) of the aldehyde (S)-I varied with time and other conditions; typical products were the carbinolamine II and the amine III, but in no case was the earlier reported ketone IV obtained. Reductive cyclization of the racemic aldehydes V (R, R1, R2, R3 = H, H, Me, OH; H, H, H, Me; H, Me, H, H; Me, H, H, H; H, H, H, MeO) was also studied under a variety of conditions.

IT **100231-11-6P 100231-12-7P 100231-13-8P**
100231-14-9P 100296-65-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

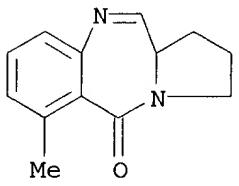
RN 100231-11-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methyl- (9CI) (CA INDEX NAME)



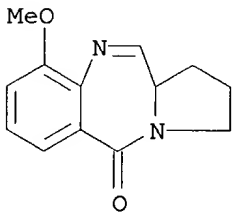
RN 100231-12-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



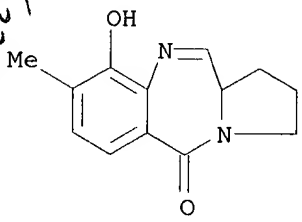
RN 100231-13-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-6-methyl- (9CI) (CA INDEX NAME)



RN 100231-14-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy- (9CI) (CA INDEX NAME)

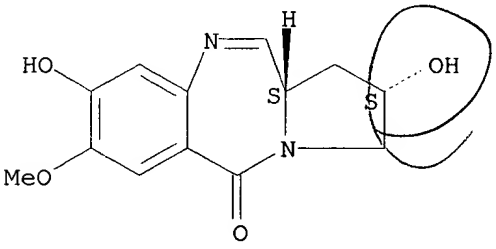


RN 100296-65-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-8-methyl- (9CI) (CA INDEX NAME)

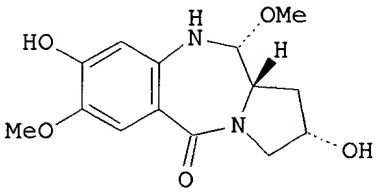


L26 ANSWER 78 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1984:468945 CAPLUS
DN 101:68945
TI Chicamycin, a new antitumor antibiotic. I. Production, isolation and properties
AU Konishi, Masataka; Hatori, Masami; Tomita, Koji; Sugawara, Masaru; Ikeda, Chiharu; Nishiyama, Yuji; Imanishi, Hideyo; Miyaki, Takeo; Kawaguchi, Hiroshi
CS Bristol-Banyu Res. Inst., Ltd., Tokyo, Japan
SO J. Antibiot. (1984), 37(3), 191-9
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
AB Chicamycin is a new antitumor antibiotic produced by a strain of Streptomyces albus, no. J576-99. The antibiotic is extractable into org. solvents from the fermn. broth and is obtained in 2 active forms, chicamycins A and B; the form depends upon the isolation procedure used. Chicamycin A is not a natural antibiotic but the MeOH adduct of naturally produced chicamycin B. Both forms of the antibiotic have weak antibacterial activity against some gram-pos. and acid-fast bacteria. They inhibit the growth of exptl. tumors, such as P388 mouse leukemia.
IT **89675-39-8**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(from Streptomyces albus, antitumor activity of)
RN 89675-39-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2S,11aS)- (9CI) (CA INDEX NAME)

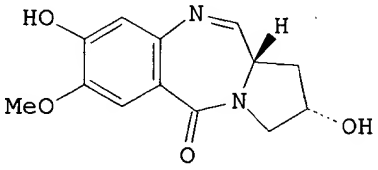
Absolute stereochemistry.



L26 ANSWER 79 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1984:420267 CAPLUS
DN 101:20267
TI Chicamycin, a new antitumor antibiotic. II. Structure determination of chicamycins A and B
AU Konishi, Masataka; Ohkuma, Hiroaki; Naruse, Nobuaki; Kawaguchi, Hiroshi
CS Bristol-Banyu Res. Inst., Ltd., Tokyo, Japan
SO J. Antibiot. (1984), 37(3), 200-6
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI



I

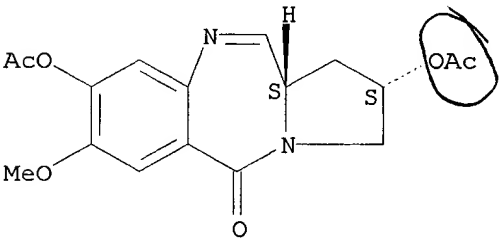


II

AB Structures of chicamycins A (I) and B (II) were detd. from a series of chem. degrdn. studies coupled with spectroscopic anal. The structure of II is closely related to neothramycin, differing only in the position of a hydroxyl substituent on the pyrrolidine ring.

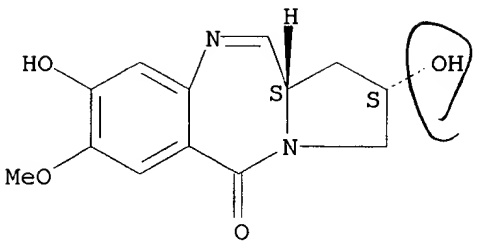
IT **90569-56-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 90569-56-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2,8-bis(acetyloxy)-1,2,3,11a-tetrahydro-7-methoxy-, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **89675-39-8**
RL: PRP (Properties)
(structure of, antitumor antibiotic activity in relation to)
RN 89675-39-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2S,11aS)- (9CI) (CA INDEX NAME)

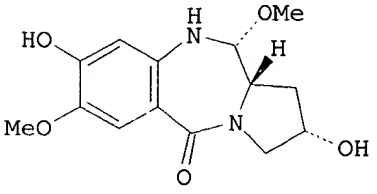
Absolute stereochemistry.


HO
N
H
S
S
OH
N
MeO
O

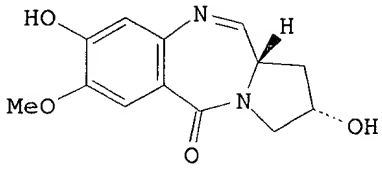
L26 ANSWER 80 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1984:405551 CAPLUS
DN 101:5551
TI Antitumor antibiotics
IN Hatori, Masami; Ohkuma, Hiroaki; Konishi, Masataka; Miyaki, Takeo; Kawaguchi, Hiroshi
PA Bristol-Myers Co. , USA
SO Eur. Pat. Appl., 53 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 101924	A1	19840307	EP 1983-107303	19830725
EP 101924	B1	19880921		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4464467	A	19840807	US 1982-401469	19820726
CA 1213542	A1	19861104	CA 1983-430626	19830617
AT 37394	E	19881015	AT 1983-107303	19830725
JP 59036678	A2	19840228	JP 1983-135283	19830726
JP 05021909	B4	19930325		
US 4508647	A	19850402	US 1984-608736	19840510
JP 05076350	A2	19930330	JP 1991-305643	19911025
PRAI US 1982-401469		19820726		
EP 1983-107303		19830725		

GI



I



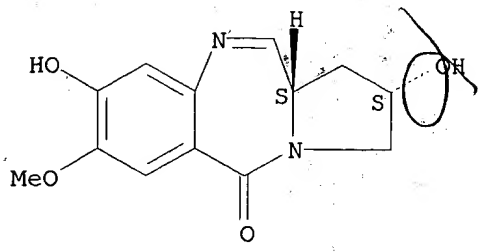
II

AB Two new antibiotics, designated BBM-2040A (I) [89675-37-6] and BBM-2040B (II) [**89675-39-8**], are produced by aerobic fermn. of Streptomyces species strain J576-99 in a medium contg. 3% soybean meal, 2% corn starch, 1% CaCO3, and 0.33% MgSO4.7H2, pH 7.0, at 28.degree. for 120 h. I was isolated from the culture filtrate by extn. with MeOH and purified by column chromatog. II was isolated by extn. with a nonmethanolic solvent such as BuOH, followed by column chromatog. and TLC at 5.degree.. Both I and II were recovered in their desmethanol or methanol adduct form. The yields of I and II were 1.10 and 3.30 g, resp. The antibiotics inhibited gram-pos. and acid-fast bacteria and slowed the growth of tumors such as P388 leukemia in mice.

IT **89675-39-8**
RL: BIOL (Biological study)
(antitumor antibiotic, from Streptomyces)

RN 89675-39-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2S,11aS)- (9CI) (CA INDEX NAME)

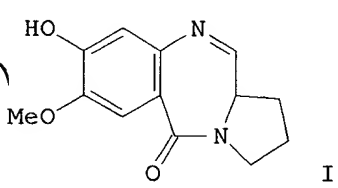
Absolute stereochemistry.


HO
N
H
OH
S
S
N
MeO
O

L26 ANSWER 81 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1984:173150 CAPLUS
DN 100:173150
TI Antibiotic DC-81
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58180487	A2	19831021	JP 1982-63630	19820416

GI



I

AB Antibiotic DC-81 (I) [**89824-22-6**] is isolated from cultures of Streptomyces roseiscleroticus DC-81. Thus, the microorganism was cultured at 30.degree. for 72 h on a medium contg. dextrin 50, soybean meal 20, KH2PO4 0.5, MgSO4.7H2O 0.5, and CaCO3 5 g/L and filtered.

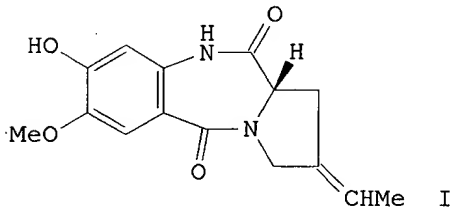
IT **89824-22-6**
RL: BIOL (Biological study)
(antibiotic, from Streptomyces roseiscleroticus)

RN 89824-22-6 CAPLUS

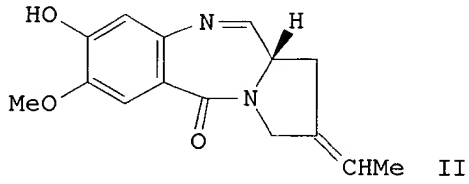
L26 ANSWER 82 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1984:156434 CAPLUS
DN 100:156434
TI Conversion of oxotomaymycin to tomaymycin
IN Kaneko, Takushi; Wong, Henry S. L.
PA Bristol-Myers Co. , USA
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4427588	A	19840124	US 1982-439965	19821108
	JP 59101486	A2	19840612	JP 1983-208436	19831108
	JP 05024157	B4	19930406		
PRAI	US 1982-439965		19821108		

GI



I



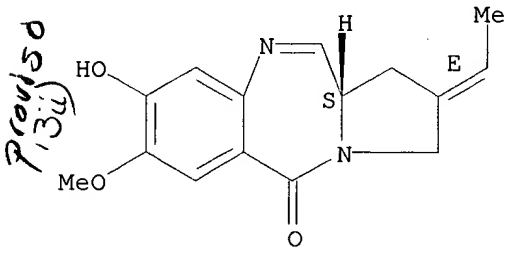
II

AB Oxotomaymycin (I) was converted to demethanoltomaymcin (II) by benzoylation, thiolation, S-methylation, methoxylation of the methylthio deriv., redn. of the imino ether bond, and elimination of MeOH.

IT **81422-30-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

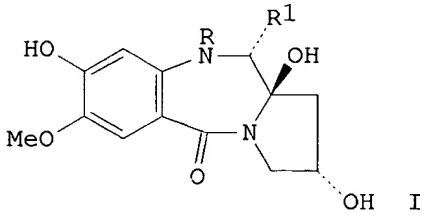
Absolute stereochemistry.
Double bond geometry as shown.



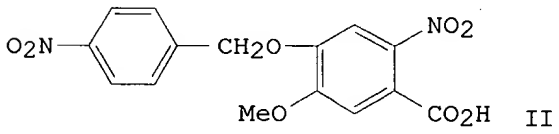
L26 ANSWER 83 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1984:156433 CAPLUS
DN 100:156433
TI Total synthesis of antitumor antibiotics BBM-2040A and BBM-2040B
IN Kaneko, Takushi; Wong, Henry S. L.
PA Bristol-Myers Co. , USA
SO U.S., 23 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4427587	A	19840124	US 1982-440779	19821110
	EP 109047	A1	19840523	EP 1983-111195	19831109
	EP 109047	B1	19871104		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 30591	E	19871115	AT 1983-111195	19831109
	JP 59101487	A2	19840612	JP 1983-210023	19831110
	JP 05016430	B4	19930304		
	JP 05247046	A2	19930924	JP 1992-88431	19920227
	JP 07020962	B4	19950308		
PRAI	US 1982-440779		19821110		
	EP 1983-111195		19831109		

GI



I



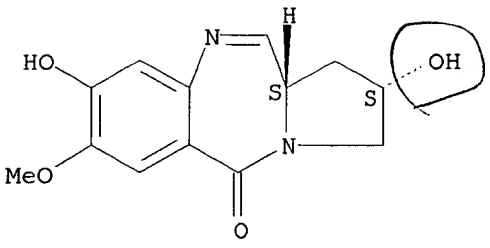
II

AB The title compds. I (R = H, R1 = OMe; RR1 = bond) were prepd. from trans-4-hydroxy-L-proline and benzoic acid II in 9 steps. I had significant antitumor activity at 3 mg/kg day i.p. in mice.

IT **89675-39-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antitumor activity of)

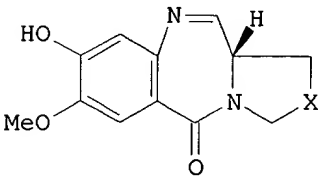
RN 89675-39-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

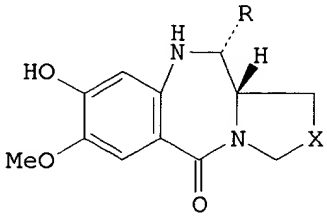

HO
N
H
S
S
OH
N
MeO
O

see 59 of 107

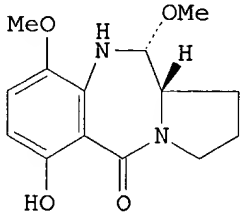
L26 ANSWER 84 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1984:138816 CAPLUS
DN 100:138816
TI Studies on tomaymycin. III. Syntheses and antitumor activity of tomaymycin analogs
AU Tozuka, Zenzaburo; Yazawa, Hisatoyo; Murata, Masayoshi; Takaya, Takao
CS Res. Lab., Fujisawa Pharm. Co., Ltd., Osaka, Japan
SO J. Antibiot. (1983), 36(12), 1699-708
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI



I



II



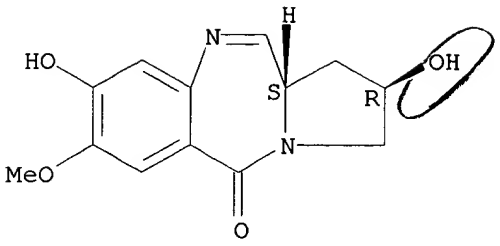
III

AB Analogs I-III [X = CH2, CH2CH2, S, CHOH, CO, CHO2C(CH2)14Me, CO, C:NOMe, C:CHCN, C:CHMe; R = OMe, NEt2, SEt, SCH2Ph] of tomaymycin (II, X = C:CHMe, R = OMe) were prepd. Most of them were inactive against leukemia P388 in mice and the activity of the others was less than that of tomaymycin. Only the O-Me deriv. of tomaymycin had antileukemic activity comparable to that of the parent.

IT **85993-77-7**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antitumor activity of)

RN 85993-77-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2R-cis)- (9CI) (CA INDEX NAME)

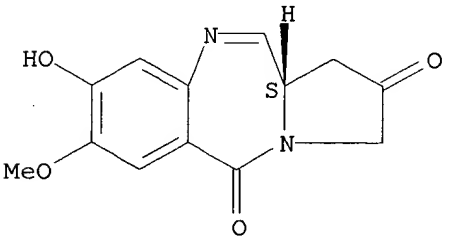
Absolute stereochemistry.



IT **81306-73-2P 81307-24-6P 89300-07-2P**
89300-08-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antitumor activity of)

RN 81306-73-2 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione, 8-hydroxy-7-methoxy-, (S)- (9CI) (CA INDEX NAME)

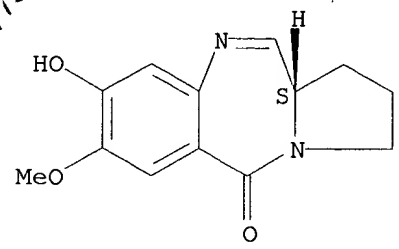
Absolute stereochemistry.



RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

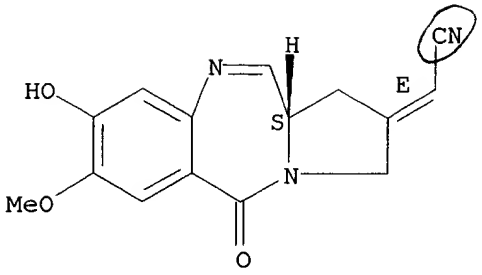
Absolute stereochemistry.

PROVISO



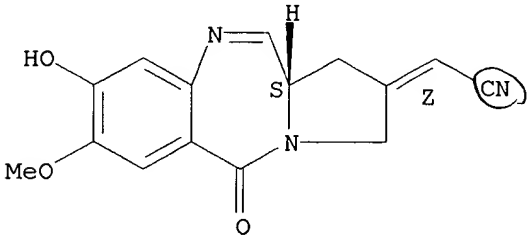
RN 89300-07-2 CAPLUS
CN Acetonitrile, (5,11a-dihydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene)-, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



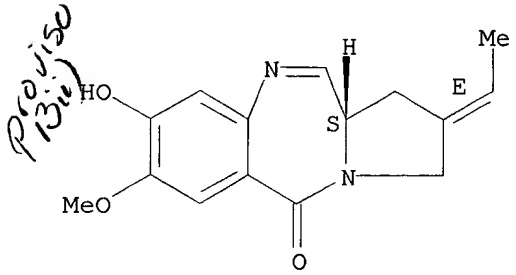
RN 89300-08-3 CAPLUS
CN Acetonitrile, (5,11a-dihydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene)-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



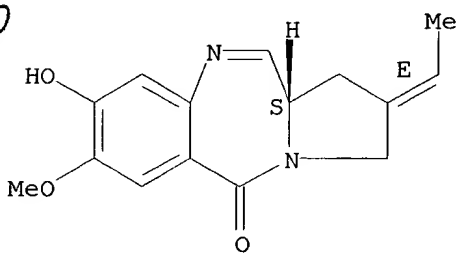
IT **81422-30-2**
RL: RCT (Reactant)
(reaction of, with thiols)
RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



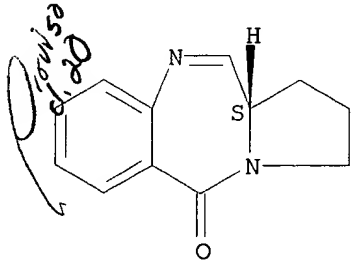
L26 ANSWER 85 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1984:138814 CAPLUS
DN 100:138814
TI A new and mild method for the reduction of secondary amides to carbinolamine ethers and imines: a conversion of oxotomaymycin to tomaymycin
AU Kaneko, T.; Wong, H.; Doyle, T. W.
CS Pharm. Res. Dev. Div., Bristol-Myers Co., Syracuse, NY, 13221-4755, USA
SO Tetrahedron Lett. (1983), 24(47), 5165-8
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
AB Secondary carboxamides were reduced to the corresponding amines by thiolation, iminoalkylation, and Al-Hg redn. of the intermediate thiol ethers. Thus, oxotomaymycin was converted to the thione, S-methylated, and reduced with AlHg in aq. THF to give pretomaymycin which was methanolyzed with MeOH at <0.degree. to give tomaymycin (I).
IT **81422-30-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and methanolysis of)
RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **72435-89-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

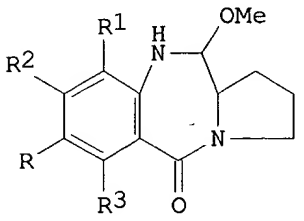
Absolute stereochemistry. Rotation (+).



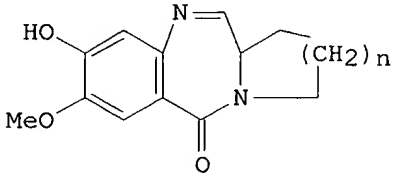
L26 ANSWER 86 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1983:539984 CAPLUS
DN 99:139984
TI Benzodiazepine derivatives
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 58041878	A2	19830311	JP 1981-141503	19810907

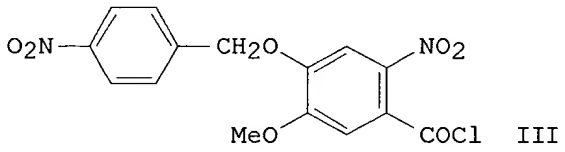
GI



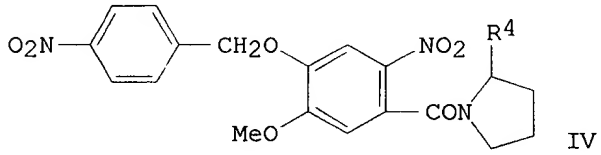
I



II



III



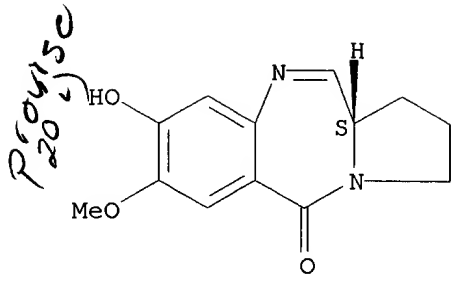
IV

AB I (R-R3 = MeO, H, OH, H; H, MeO, H, OH) and II (n = 1,2) were prepd. and tested for anticarcinogenic activity on mouse leukemia cells P388. Thus, condensation of III with L-proline in THF contg. Et3N at room temp. gave IV (R4 = CO2H), hydride redn. gave IV (R4 = CHO), and hydrogenolysis in MeOH-EtOAc contg. Pd/BaSO4 at room temp. for 4 h gave I (R-R3 = MeO, H, OH, H) and II (n = 1).

IT **81307-24-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antileukemia activity of)

RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

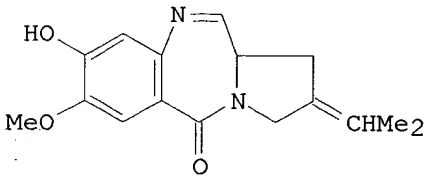
Absolute stereochemistry.


HO
MeO
N
H
S
N
O

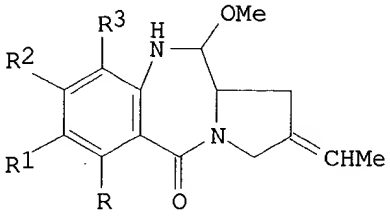
L26 ANSWER 87 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1983:539983 CAPLUS
DN 99:139983
TI Benzodiazepine derivatives
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 58041884	A2	19830311	JP 1981-141502	19810907

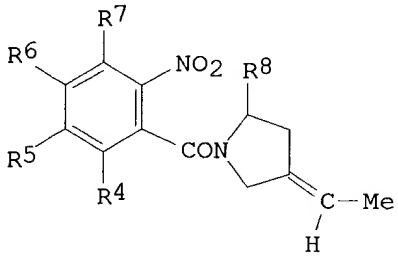
GI



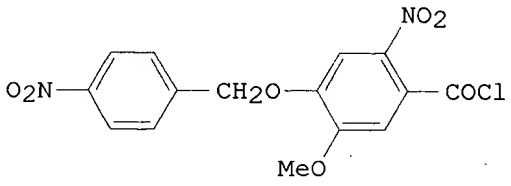
I



II



III



IV

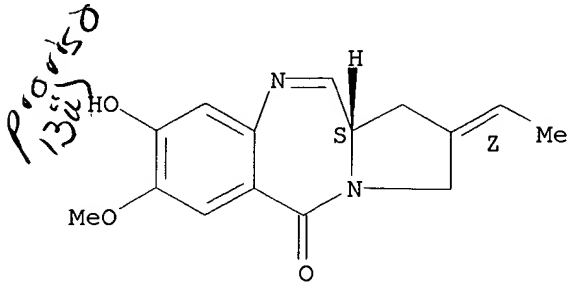
AB Antibacterial and anticarcinogenic (no data) benzodiazepine derivs. I and II (R = R3 = H, R1 = Me, R2 = HO; R = R3 = HO, R1 = R2 = H) were prepd. by reductive cyclization of III [R4-R7 = H, MeO, (protected) HO; R8 = CHO]. Thus, reaction of N-(tert-butoxycarbonyl)-4-oxo-L-proline Ph2CH ester with EtPh3PBr followed by deprotection gave (4Z)-ethylidene-L-proline Ph2CH ester, whose acylation with IV in EtOAc contg. Et3H at room temp. gave III (R4 = R7 = H, R5 = MeO, R6 = PhCH2O, R8 = CO2CHPh2), treatment of which with F3CCO2H in PhOMe at room temp. gave the corresponding III (R8 = CO2H), whose hydride redn. gave III (R8 = CHO), hydrogenation of which over Pd/BaSO3 at room temp. for 3 h gave (2Z,11aS)-I.

IT **81422-29-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

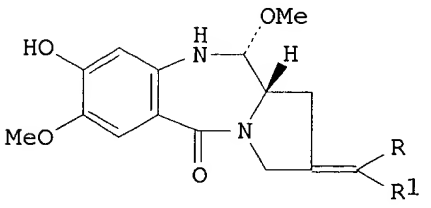
RN 81422-29-9 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

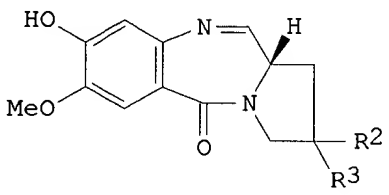
Absolute stereochemistry.
Double bond geometry as shown.



L26 ANSWER 88 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1983:422186 CAPLUS
DN 99:22186
TI Studies on tomaymycin. II. Total syntheses of the antitumor antibiotics, E- and Z-tomaymycins
AU Tozuka, Zenzaburo; Takasugi, Hisashi; Takaya, Takao
CS Res. Lab., Fujisawa Pharm. Co., Ltd., Osaka, Japan
SO J. Antibiot. (1983), 36(3), 276-82
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI



I



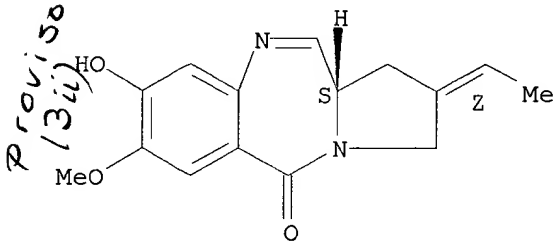
II

AB Naturally occurring E-tomaymycin (I, R = Me, R1 = H) and its Z-isomer (I, R = H, R1 = Me) were prepd. from hydroxyproline. Unsatd. analogs II (R2 = OH, R3 = H; R2R3 = CHMe) were also prepd. Z-I had the same antibacterial activity as E-I.

IT **81422-29-9P 81422-30-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and methanolysis of)

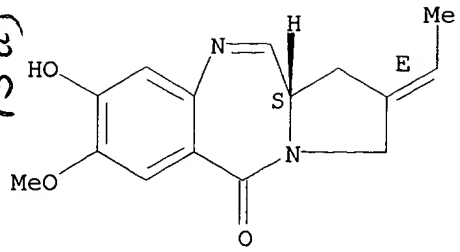
RN 81422-29-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



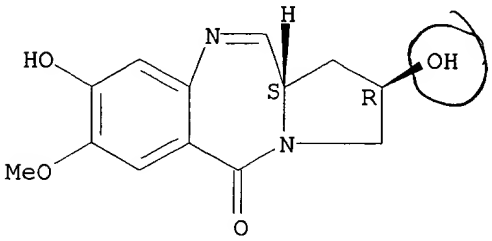
RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **85993-77-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 85993-77-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2R-cis)- (9CI) (CA INDEX NAME)

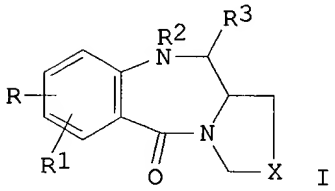
Absolute stereochemistry.

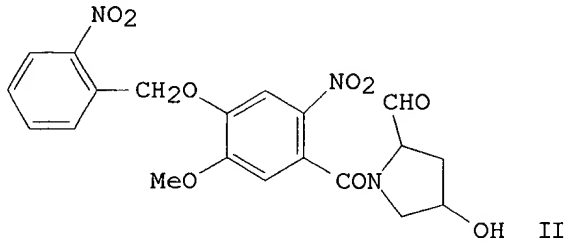


L26 ANSWER 89 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1983:72145 CAPLUS
DN 98:72145
TI Benzodiazepine derivatives
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 57131791	A2	19820814	JP 1981-216205	19811228
	JP 02016315	B4	19900416		
PRAI	GB 1980-41626		19801231		

GI

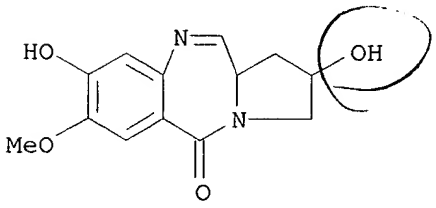

I


II

AB Title compds. I (R = OH; R1 = alkoxy; R2 = H; R3 = alkoxy; R2R3 = bond; X = CHOH, S, CO, C:CHCN, C:NR5, R5 = alkoxy), useful as bactericides, and antineoplastics (data given), were prepd. Thus, reductive cyclization of pyrrolidine II with 10% Pd/C gave I (R = 8-OH, R1 = 7-MeO, R2R3 = bond, X = CHOH).

IT **81306-70-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antineoplastic activity of)

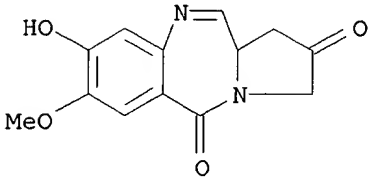
RN 81306-70-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy- (9CI) (CA INDEX NAME)



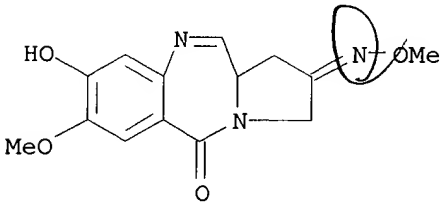
IT **84447-45-0P 84447-47-2P 84447-48-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 84447-45-0 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione,

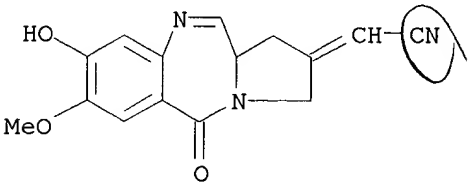
8-hydroxy-7-methoxy- (9CI) (CA INDEX NAME)



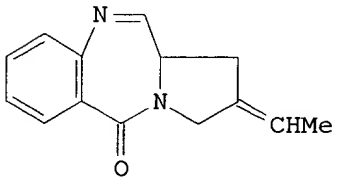
RN 84447-47-2 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione, 8-hydroxy-7-methoxy-, 2-(O-methyloxime) (9CI) (CA INDEX NAME)



RN 84447-48-3 CAPLUS
CN Acetonitrile, (5,11a-dihydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene)- (9CI) (CA INDEX NAME)



L26 ANSWER 90 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1982:578414 CAPLUS
DN 97:178414
TI Prothracarcin, a novel antitumor antibiotic
AU Shimizu, Kenichi; Kawamoto, Isao; Tomita, Fusao; Morimoto, Makoto; Fujimoto, Kazuhisa
CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co. Ltd., Tokyo, Japan
SO J. Antibiot. (1982), 35(8), 972-8
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI

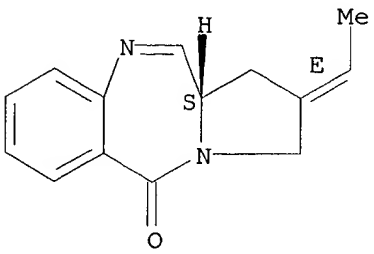


I

AB A novel antibiotic, prothracarcin (I), was isolated from the culture broth of Streptomyces umbrosus raffinophilus DO-62. The antibiotic has the mol. formula C14H14N2O and belongs to the pyrrolo[1,4]benzodiazepine antibiotics. Its structure was elucidated by mass and NMR spectra. It is active against gram-pos. and gram-neg. bacteria and exptl. murine tumor sarcoma 180 and leukemia P388.

IT **81542-99-6**
RL: BIOL (Biological study)
(antibiotic, from Streptomyces umbrosus)
RN 81542-99-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (2E,11aS)- (9CI) (CA INDEX NAME)

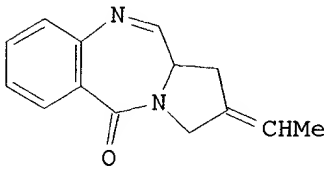
Absolute stereochemistry.
Double bond geometry as shown.



L26 ANSWER 91 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1982:179428 CAPLUS
DN 96:179428
TI Antibacterial and anticarcinogenic DC-62
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 56158785	A2	19811207	JP 1980-62256	19800513
	JP 63030916	B4	19880621		

GI



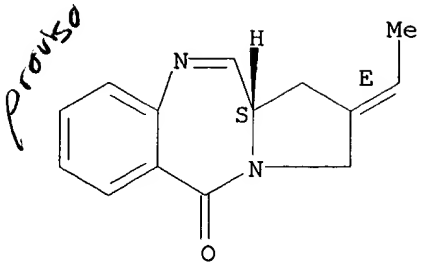
I

AB Antibacterial and anticarcinogenic DC-62 (I) was prepd. by cultivation of Streptomyces umbrosus raffinophilus DC-62 and isolated from the culture broth. Min. inhibitory concns. of I were 50, 50, 50, >100, and >100 .mu.g/mL against Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Sarcina typhosa, and Shigella sonnei, resp. Anticarcinogenic activity of I was demonstrated against Sarcoma 180 solid tumor and lymphocytic leukemia P-388 tumor cells, in mice; LD50 of I was 42 mg/kg i.p. in mice. Thus, precultured S. umbrosus raffinophilus (Bikoken 5468, NRRL 12143) was cultured on 15 L broth (pH 7) comprising molasses 10 (as glucose), corn steep liquor 10, NaCl 1, KCl 10, MnSO4.cntdot.H2O 2, NH4H2PO4 1, and L-lysine 40 g/L for 72 h at 30.degree. under 15 L/min aeration. I was chromatographed over Diaion HP-10 and Sephadex LH-20 to yield 10 mg I. The IR spectra of I are presented.

IT **81542-99-6**
RL: BIOL (Biological study)
(from Streptomyces umbrosus, as tumor inhibitor)
RN 81542-99-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

Provisional



see 89 9107

L26 ANSWER 92 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1982:162399 CAPLUS
DN 96:162399
TI Syntheses of tomaymycin and its analogs
AU Tozuka, Zenzaburo; Takaya, Takao
CS Res. Lab., Fujisawa Pharm. Co. Ltd., Japan
SO Tennen Yuki Kagobutsu Toronkai Koen Yoshishu, 24th (1981), 552-9
Publisher: Osaka Univ., Fac. Pharm. Sci., Suita, Japan.
CODEN: 47BNAB
DT Conference
LA Japanese
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

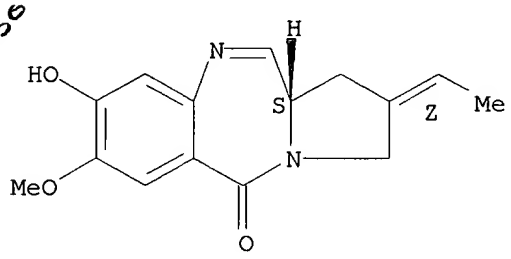
AB Tomaymycin [(E)-I] and (Z)-I were prepd. from L-hydroxyproline (II) and vanillin (III) in several steps. Proline IV was acylated with acid chloride V to give benzoylproline VI (R = OCHPh2), which was converted to VI (R = H), which was converted to (E)- and (Z)-I or to dehydro derivs. (E)- and (Z)-VII. IV and V were prepd. from II and III, resp. The structure and configuration of (E)-I were detd. by H and 13C NMR data. Several tomaymycin analogs were also prepd.

IT **81422-29-9P 81422-30-2P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and NMR of)

RN 81422-29-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

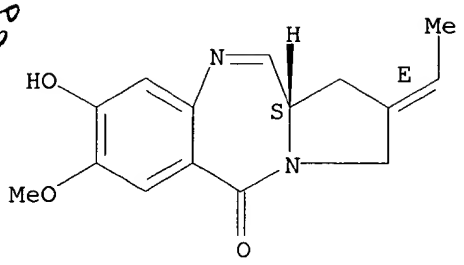
Absolute stereochemistry.
Double bond geometry as shown.

Provisional

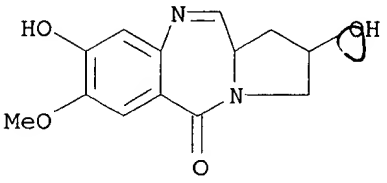


RN 81422-30-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

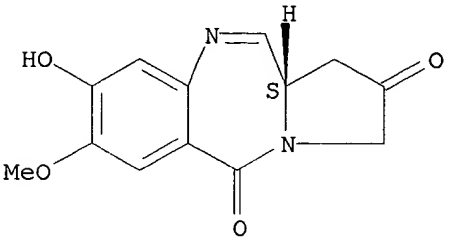


IT **81306-70-9P 81306-73-2P 81306-74-3P**
81306-75-4P 81306-76-5P 81306-77-6P
81307-24-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 81306-70-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy- (9CI) (CA INDEX NAME)



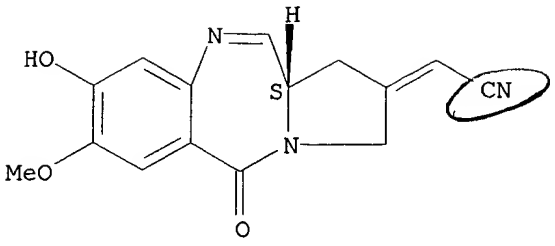
RN 81306-73-2 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione, 8-hydroxy-7-methoxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



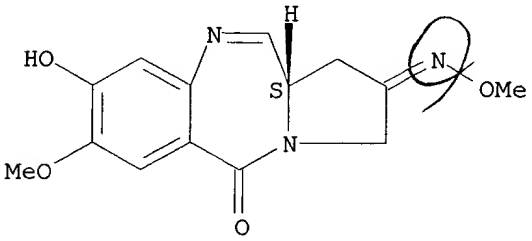
RN 81306-74-3 CAPLUS
CN Acetonitrile, (5,11a-dihydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



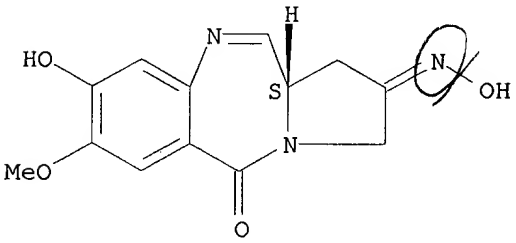
RN 81306-75-4 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione, 8-hydroxy-7-methoxy-, 2-(O-methyloxime), (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



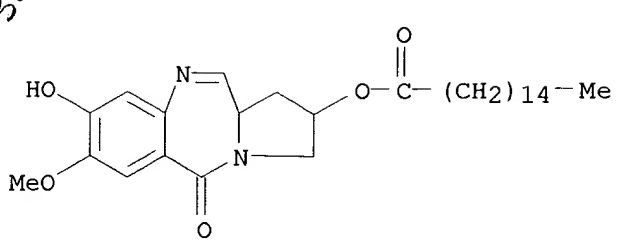
RN 81306-76-5 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione, 8-hydroxy-7-methoxy-, 2-oxime, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 81306-77-6 CAPLUS
CN Hexadecanoic acid, 2,3,5,11a-tetrahydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl ester (9CI) (CA INDEX NAME)

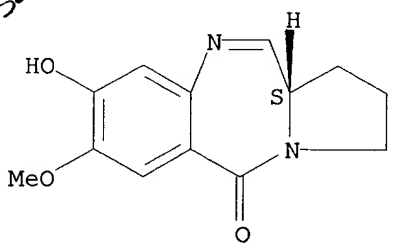
proviso



RN 81307-24-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

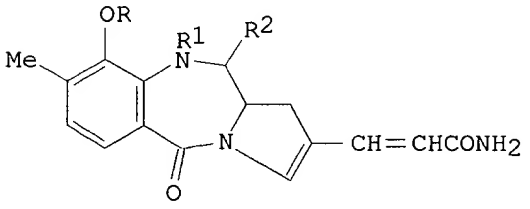
Prov.so



L26 ANSWER 93 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1981:139855 CAPLUS
DN 94:139855
TI Benzodiazepines
PA Green Cross Corp., Japan
SO Belg., 24 pp.
CODEN: BEXXAL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 882305	A1	19800716	BE 1980-199851	19800319
	JP 56015289	A2	19810214	JP 1979-89886	19790717
	JP 62037631	B4	19870813		
	SE 8001458	A	19810118	SE 1980-1458	19800225
	SE 436882	B	19850128		
	SE 436882	C	19850509		
	CA 1152985	A1	19830830	CA 1980-346511	19800227
	US 4309437	A	19820105	US 1980-127984	19800304
	GB 2053894	A	19810211	GB 1980-8033	19800310
	GB 2053894	B2	19830420		
	NL 8001531	A	19810120	NL 1980-1531	19800314
	DE 3010544	A1	19810129	DE 1980-3010544	19800319
	DE 3010544	C2	19820701		
	FR 2461711	A1	19810206	FR 1980-6153	19800319
	FR 2461711	B1	19830513		
	CH 648848	A	19850415	CH 1980-2187	19800320
PRAI	JP 1979-89886		19790717		

GI



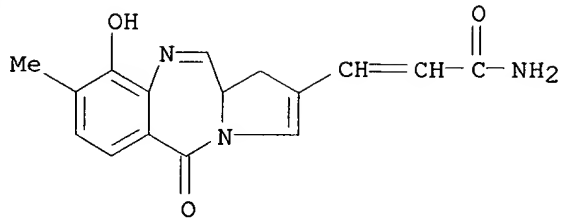
I

AB Pyrrolobenzodiazepines I (R = H, acyl, CONH2, alkoxycarbonyl; R1 = H, acyl; R2 = SO2H) were prepd. by treating I (R2 = OMe) with Na dithionite. I (R2 = SO3H) were prepd. by oxidizing I (R2 = SO2H) or by treating I (R2 = OMe) with SO2 or K2SO3. Thus, 1 g I (R = R1 = Ac, R2 = OMe) was treated with Na dithionite to give 0.8 g I (R = R1 = Ac, R2 = SO2H), which at 0.12 mg/kg daily i.p. for 6 days increased the survival time of leukemia P388 infected mice by 190%.

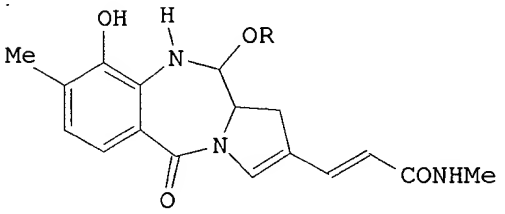
IT **14435-72-4**
RL: RCT (Reactant)
(sulfination of)

RN 14435-72-4 CAPLUS
CN 2-Propenamide, 3-(5,10,11,11a-tetrahydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)- (9CI) (CA INDEX NAME)

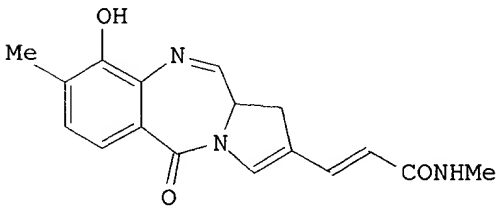
Prov150



L26 ANSWER 94 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1980:636828 CAPLUS
DN 93:236828
TI Mazethramycin, a new member of anthramycin group antibiotics
AU Kunimoto, Setsuko; Masuda, Toru; Kanbayashi, Nobuo; Hamada, Masa; Naganawa, Hiroshi; Miyamoto, Masashi; Takeuchi, Tomio; Umezawa, Hamao
CS Inst. Microbial Chem., Tokyo, 141, Japan
SO J. Antibiot. (1980), 33(6), 665-7
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI



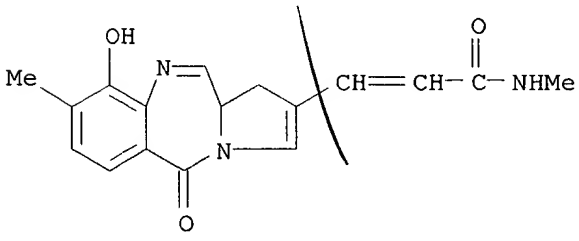
I, R=H
II, R=Me
III, R=Et



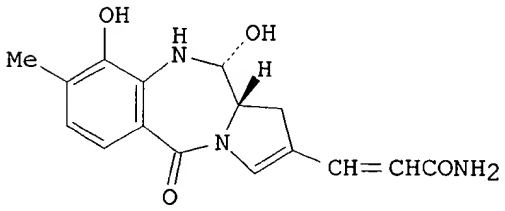
IV

AB Mazethramycin (I) [68373-96-6] was produced by fermn. with Streptomyces thioluteus. The Me ether (II) [68373-95-5], Et ether (III) [68373-94-4], and anhydro (IV) [**68373-93-3**] derivs. were obtained by chem. treatment. II inhibited gram-pos. and gram-neg. bacteria and prolonged the survival of mice infected with leukemia L-1210 cells.

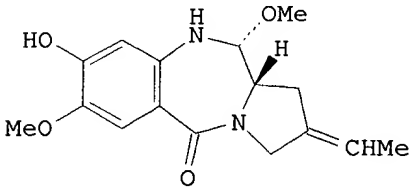
IT **68373-93-3P**
RL: PREP (Preparation)
(prepn. of)
RN 68373-93-3 CAPLUS
CN 2-Propenamide, 3-(5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)-N-methyl- (9CI) (CA INDEX NAME)



L26 ANSWER 95 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1980:51709 CAPLUS
DN 92:51709
TI Antitumor antibiotics. XVI. Molecular mechanism of binding of pyrrolo(1,4)benzodiazepine antitumor agents to deoxyribonucleic acid. Anthramycin and tomaymycin
AU Lown, J. William; Joshua, Alummoottil V.
CS Dep. Chem., Univ. Alberta, Edmonton, AB, T6G 2G2, Can.
SO Biochem. Pharmacol. (1979), 28(13), 2017-26
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
GI



I

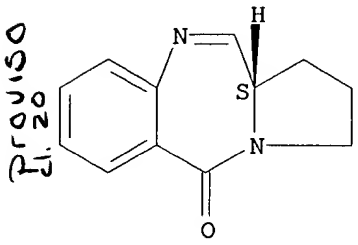


II

AB The extent of binding of the pyrrolo[1,4]benzodiazepine antibiotics, anthramycin (I) [4803-27-4] and tomaymycin (II) [35050-55-6], to DNA, measured by suppression of ethidium fluorescence, was proportional to the antibiotic concn. and was partly reversed by a heat-denaturation-renaturation cycle. The extent of binding of I and II to DNA was promoted by lower pH (4.7-9) and higher temps. (0-51.degree.), and the DNA-antibiotic complex was stable to dialysis. There was no evidence that these antibiotics intercalate into DNA, but they were more reactive toward relaxed PM2-DNA than to supercoiled DNA. Examn. of DNA binding of the antibiotics and their analogs to DNAs of different base compn. and sep. in conjugation with sequence specific binding agents showed little base preference for binding. Reaction of the antibiotics with DNA produced neither depurination nor strand scission. A free or potential carbinolamine or imine function at the 10,11 positions in a benzo[1,4]diazepine nucleus was an abs. requirement for DNA binding or of reaction with nucleophiles.

IT **72435-89-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and DNA binding to, antitumor activity in relation to)
RN 72435-89-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

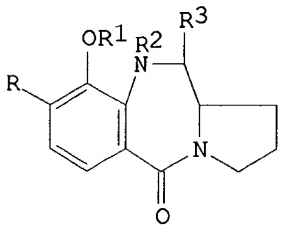


Provisional 20

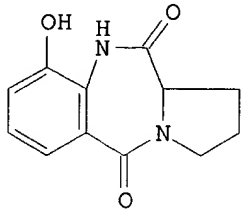
L26 ANSWER 96 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1979:540872 CAPLUS
DN 91:140872
TI Pyrrolobenzodiazepines useful in treating tumors
IN Takanabe, Atsuyuki; Arakawa, Yoshio; Kagitani, Yoshio; Ueda, Yasuo; Satoh, Daisuke; Komatsu, Nobuhiko
PA Green Cross Corp., Japan
SO Ger. Offen., 45 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2844292	A1	19790628	DE 1978-2844292	19781011
	JP 54090195	A2	19790717	JP 1977-156684	19771227
	JP 58005916	B4	19830202		
	US 4185016	A	19800122	US 1978-947418	19781002
	US 4239683	A	19801216	US 1979-42449	19790525
PRAI	JP 1977-156684		19771227		
	US 1977-947418		19771002		

GI



I



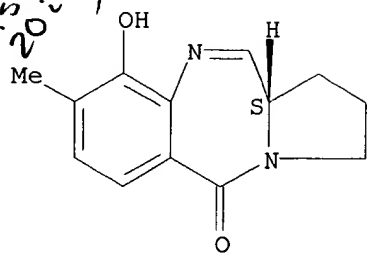
II

AB The pyrrolobenzodiazepines I (R = H, OH, alkyl, alkoxy; R1 = H, acyl; R2R3 = bond; R2 = H, R3 = OR4; R4 = H, alkyl, phenylalkyl) were prepd. and tested for antitumor activity (test data tabulated). Thus, L-proline Me ester reacted with 3,2-(HO)(O2N)C6H3CO2H, and the product was hydrogenated, followed by refluxing in xylene to give II. This was treated with PhCH(OMe)2, followed by reaction with NaBH4 in MeOH to give I (R-R2 = H, R3 = OMe), which at 5 mg/kg prolonged the life of mice infected with Leukemia P388 by 148.0%.

IT **71444-82-1P 71444-83-2P 71444-84-3P**
71444-90-1P 71445-00-6P 71445-01-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antitumor activity of)

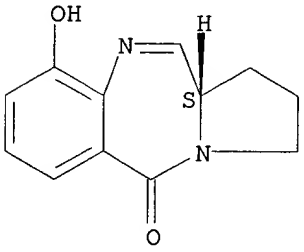
RN 71444-82-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-8-methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



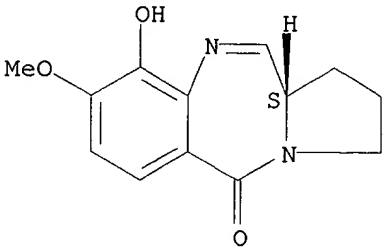
RN 71444-83-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



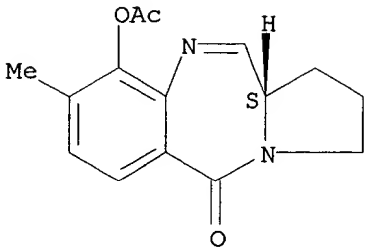
RN 71444-84-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-8-methoxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



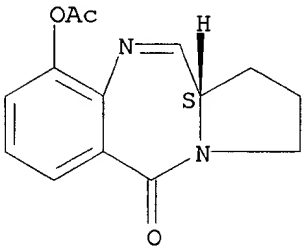
RN 71444-90-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-(acetyloxy)-1,2,3,11a-tetrahydro-8-methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



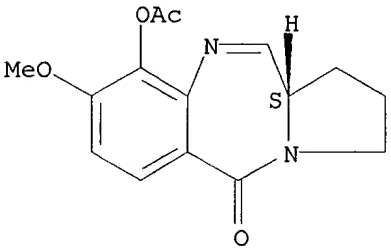
RN 71445-00-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-(acetyloxy)-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 71445-01-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-(acetyloxy)-1,2,3,11a-tetrahydro-8-methoxy-, (S)- (9CI) (CA INDEX NAME)

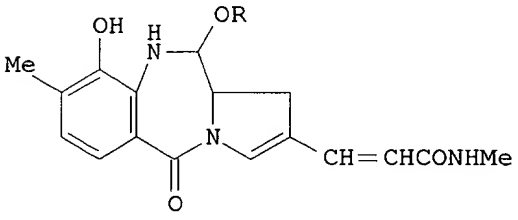
Absolute stereochemistry.



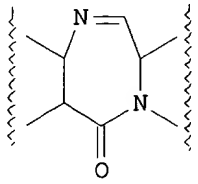
L26 ANSWER 97 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1979:4427 CAPLUS
DN 90:4427
TI Mazethramycins
IN Umezawa, Hamao; Takeuchi, Tomio; Hamada, Masashi; Kunimoto, Setsuko
PA Microbiochemical Research Foundation, Japan
SO Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 53082792	A2	19780721	JP 1976-157479	19761228
JP 60053033	B4	19851122		

GI



I, R=H
II, R=Me
III, R=Et

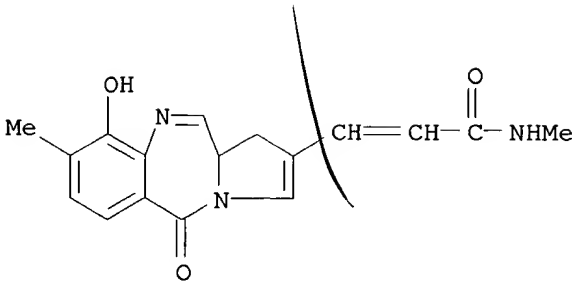


IV

AB Mazethramycin A (I) [68373-96-6], mazethramycin B (II) [68373-95-5], mazethramycin C (III) [68373-94-4], and anhydromazethramycin (IV) [**68373-93-3**] were prepd. by cultivation of Streptomyces thioluteus ME 561-14 followed by chem. treatment. I-IV had antibacterial and antileukemic activities. Thus, S. thioluteus ME 561-14 was precultured on a liq. broth of glycine 1.5, cottonseed meal 1.5, L-asparagine 0.2, and NaCl 0.3% for 48 h at 27.degree. and then cultured for 4 days at 27.degree. to give 216 mg I-IV in the culture. The culture was made pH 8.0, extd. with BuOH, dissolved in H2O, and chromatographed on Amberlite XAD and SiO2 gel to give 71 mg II. Refluxing 124 mg II with Amberlite CG-80 in MeCN for 1 h gave 80 mg IV, which was dissolved in 50% aq. Me2CO and concd. to give I, which (50 mg) was dissolved in EtOH and concd. to give 45 mg III. IR and UV spectra of I-III and the NMR spectrum of II are given.

IT **68373-93-3**
RL: BIOL (Biological study)
(antibiotic, from Streptomyces thioluteus)

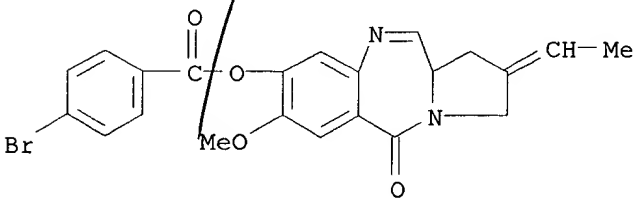
RN 68373-93-3 CAPLUS
CN 2-Propenamide, 3-(5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)-N-methyl- (9CI) (CA INDEX NAME)


OH
Me
N
N
O
CH═CH—C—NHMe
O

L26 ANSWER 98 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1975:477004 CAPLUS
DN 83:77004
TI Chemotherapeutic benzodiazepine derivatives by cultivating pretomeimycin-producing Streptomyces strain, treating with lower alcohol then nonalcoholic solvent
IN Arima, Hiroshi; Tamura, Takazo; Sakai, Heiichi; Mukosaka, Masanobu
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Japan., 14 pp. Division of Japan. Koho 73 00,076 (See Ger. 1,965,304, CA 73;77291k).
CODEN: JAXXAD
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 49025957	B4	19740704	JP 1970-99200	19701110

GI For diagram(s), see printed CA Issue.
AB Benzodiazepines (I; R = lower alkyl; R1 = halobenzoyl or H) were prepd. from pretomeimycin isolated from (or without isolation) cultures of Streptomyces by treating with lower alcs. Thus, S. achromogenes tomaymyceticus was cultured aerobically at 30.degree. for 50-60 hr in a medium contg. lactose 3, meat ext. 1, yeast 1, polypeptone 1, NaCl 0.25, KH2PO4 1.5, and Na2HPO4 0.43%. The culture was centrifuged and the supernatant was worked up to yield pretomeimycin. Pretomeimycin was dissolved in EtOAc, adsorbed on a silicate column, and eluted with EtOAc. The eluate was evapd. to near dryness. The residue was dissolved in MeOH. The soln. was allowed to stand at -20.degree. for 2 days. Ppt. formed was 2,3,5,10,11,11a-hexahydro-2-ethylidene-7,11-dimethoxy-8-hydroxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepine (I; R = Me; R1 = H).
IT **28797-41-3**
RL: PROC (Process)
(fermn. of, benzodiazepine derivs. from)
RN 28797-41-3 CAPLUS
IT **28797-41-3P 28797-43-5P**
RL: PREP (Preparation)
(prepn. of)
RN 28797-41-3 CAPLUS
RN 28797-43-5 CAPLUS
CN Benzoic acid, 4-bromo-, 2-ethylidene-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl ester (9CI) (CA INDEX NAME)



See 98 of 107

09/763,767

L26 ANSWER 99 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1975:458899 CAPLUS
DN 83:58899
TI Antibiotic pretomeimycin lower alcohol adducts having anti-microbial, anti-phage, and anti-viral activity
IN Arima, Hiroshi; Tamura, Takazo; Sakai, Heiichi; Mukosaka, Masanobu
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Japan., 12 pp. Division of Japan. Koho 73 00,076 (See Ger. 1,965,304, CA 73;77291k).
CODEN: JAXXAD
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 49025956	B4	19740704	JP 1970-99199	19701110

GI For diagram(s), see printed CA Issue.
AB Pyrrolobenzodiazepines (I, R = lower alkyl) were prepd. by treating pretomeimycin with a lower alc. or cultivating a pretomeimycin-producing Streptomyces and treating the culture medium with a lower alc. Thus, 20 g pretomeimycin in EtOAc was treated with .apprx.30 ml MeOH at -20.degree. for 2 days to give 18 g I (R = Et).
IT **28797-41-3**
RL: RCT (Reactant)
(reaction with alcs.)
RN 28797-41-3 CAPLUS

proviso 13(c)

L26 ANSWER 100 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1975:140209 CAPLUS
DN 82:140209
TI 8-Alkoxylated benzodiazepine derivatives
IN Arima, Hiroshi; Tamura, Takazo; Sakai, Heiichi; Mukosaka, Masanobu
PA Fujisawa Pharmaceutical Co., Ltd.
SO Japan., 2 pp. Division of Japan. 73 76 (See Ger. 1,965,304, CA 73: 77291k).
CODEN: JAXXAD
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 49025958	B4	19740704	JP 1970-99201	19701110

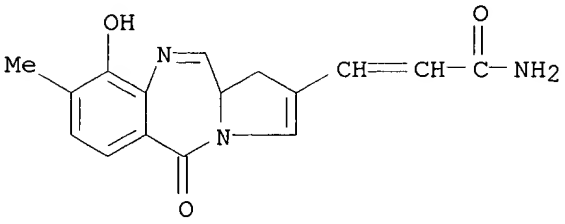
GI For diagram(s), see printed CA Issue.
AB The bactericidal and virucidal (no data) pyrrolobenzodiazepine I (R = R1 = Me) was prepd. by treating pretomeimycin with MeOH and methylating I (R = Me, R1 = H) with CH2N2.
IT **55128-21-7**
RL: RCT (Reactant)
(reaction of, with methanol)
RN 55128-21-7 CAPLUS

proviso (3 of 11)

L26 ANSWER 101 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1972:57720 CAPLUS
DN 76:57720
TI Antibiotic production utilizing Streptomyces refuineus var thermotolerans
IN Berger, Julius; Karr, Andrew E.; Leimgruber, Willy; Tabenkin, Benjamin; Schocher, Arno J.; Stefanovic, Vladimir
PA Hoffmann-La Roche Inc.
SO U.S., 9 pp. Division of U.S. 3,361,742 (CA 68;58569n).
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

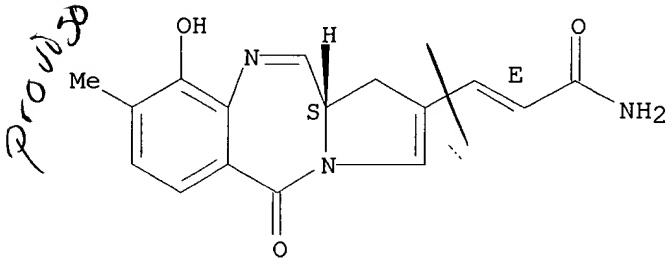
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3619374	A	19711109	US 1967-687433	19671204

AB The title bacterium (NRRL 3143 and 3144) was grown under agitated, aerobic fermentation conditions in aq. nutrient media contg. sources of carbohydrate and protein at 35-55.degree. for 12-15 hr at pH 6-8.5 and thereafter at pH 6-6.9. The culture filtrate was extd. with a solvent having low miscibility with water, esp. butanol, to yield an antibiotic-contg. ext. having antitumor and antibacterial activity.
IT **14435-72-4**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(antibiotic activity of)
RN 14435-72-4 CAPLUS
CN 2-Propenamide, 3-(5,10,11,11a-tetrahydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)- (9CI) (CA INDEX NAME)



L26 ANSWER 102 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1972:21926 CAPLUS
DN 76:21926
TI Chemosterilant action of anthramycin. Proposed mechanism
AU Horwitz, Susan B.
CS Dep. Pharmacol., Albert Einstein Coll. Med., New York, N. Y., USA
SO Science (1971), 174(4005), 159-61
CODEN: SCIEAS
DT Journal
LA English
AB The activity of anthramycin (I) [4803-27-4] and structurally related analogs as chemosterilants of the housefly, Musca domestica, correlated closely with the action of these compds. as inhibitors of Escherichia coli RNA polymerase. Since inhibition of RNA polymerase by I reflects binding of this antibiotic to the DNA primer required for enzyme activity, the interaction of I with DNA may also account for its action as a chemosterilant.
IT **16758-27-3**
RL: BIOL (Biological study)
(as chemosterilants)
RN 16758-27-3 CAPLUS
CN 2-Propenamide, 3-[(11aS)-5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

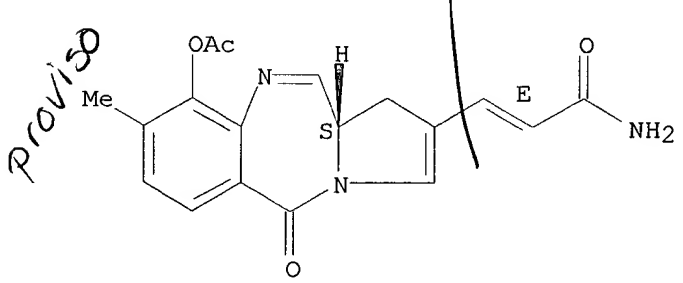


L26 ANSWER 103 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1970:531049 CAPLUS
DN 73:131049
TI Antiprotozoal, anthelmintic, and antitumor benzodiazepine compounds
IN Leimgruber, Willy; Schenker, Fausto E.
PA Hoffmann-La Roche Inc.
SO U.S., 13 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3523941	A	19700811	US 1967-620618	19670306

GI For diagram(s), see printed CA Issue.
AB The acetates of I and II were prepd. by acylation of the corresponding 9-OH deriv. I (R1 = R2 = H, R3 = .alpha.-OMe) (III), or its hydrate. The epimers of I were prepd. by acylating III, removing the elements of MeOH from the mol. by an 8 hr reflux with H2C:C(Me)OAc and treating the product with MeOH at room temp. Thus, III in 1:1 Ac2O-NEt3 stirred 4 hr at 20.degree. gave (11R,11aS)-5,10,11,11a-tetrahydro-9-hydroxy-11-methoxy-8-methyl-5-oxo- 1H-pyrrolo[2,1-c][1,4]benzodiazepine-2-trans-acrylamide acetate (IV). (11S,11aS)-Epimer of IV was similarly prepd. and had the same activity against S 180 and Ehrlich solid tumors in mice. II (R1 = H) stirred 2 hr at 20.degree. in 1:1 Ac2O-C5H5N gave II (R1 = Ac) (V). V in 4:1 H2O-Me2CO kept 18 hr at 20.degree. gave I (R1 = H, R2 = Ac, R3 = OH) (VI). V in C5H5N kept 3 days at 20.degree. in AcOH-Ac2O gave I (R1 = R2 = Ac, R3 = AcO). Treatment of III.H2O with (EtCO)2O-NEt3, (PrCO)2O-NEt2, or Bz3O-NEt3 gave I (R1 = EtCO, PrCO, or Bz). Similar acylations of III.H2O with PhNCO, EtNCO, or (EtO)2CO in the presence of NEt3 gave I (R1 = PhNHCO, EtNHCO, EtCO2). I are useful as antitumor agents against Sarcoma 180 and Ehrlich solid tumors in mice, as antiprotozoal agents against Entamoeba histolytica and Trichomonas vaginalis, and as anthelmintic agents against Syphacia obvelata.
IT **29775-04-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 29775-04-0 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acrylamide, 5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-, acetate (ester), (E)-(S)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



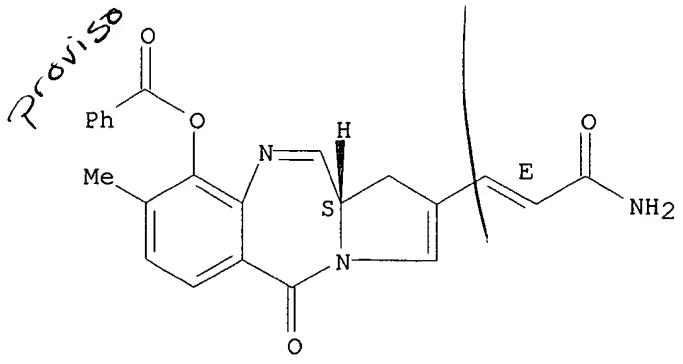
Proviso

L26 ANSWER 104 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1970:520692 CAPLUS
DN 73:120692
TI Antitumor pyrrolobenzodiazepine acrylamides and intermediates
IN Batcho, Andrew D.; Leimgruber, Willy
PA Hoffmann-La Roche Inc.
SO U.S., 12 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3524849	A	19700818	US 1967-678532	19671027

GI For diagram(s), see printed CA Issue.
AB The title antitumor agents I (R = H or Me) were prepd. from 3-benzyloxy-2-nitro-p-toluoyl chloride (II) and L-(4-hydroxyproline) Me ester (III). Thus, II was treated at 20-25.degree. with III in CH2Cl2 contg. Et3N to give 1-(3-benzyloxy-2-nitro-p-toluoyl)-L-(4-hydroxyproline) Me ester which was treated with aq. Na2S2O6 in THF at 40.degree. to give 1-(3-benzyloxy-2-amino-p-toluoyl)-L-(4-hydroxyproline) Me ester (IV). A xylene soln. of IV was refluxed overnight to give (2R,-11aS)-9-benzyloxy-1,2,3, 11a-tetrahydro-2-hydroxy-8-methyl-5H-pyrrolo[2,1-c][1,4]benzodiazepine-5, 11(10H)-dione, m. 243-3.5.degree. (vac.), which was oxidized to (11aS)-9-benzyloxy-8-methyl-1H-pyrrolo[2,1-c][1,4]benzodiazepine-2,5, 11(3H,10H,11aH)-trione (VI). Treatment of VI with Et3PCH2CO2Et gave VII (R = CO2Et). This was converted to VII (R = CHO), VII [R = CH(OH)CN], and VII [R = CH(O3SMe)CN], which gave VIII when treated with base. The reaction between VIII and F3C-CO2H gave the 9-OH analog of VIII which was treated with PhCH(OMe)2 to give IX (R = CN). IX (R = CN) was hydrolyzed in polyphosphoric acid to IX (R = CONH2) which was reduced with LiAlH4-THF at -50.degree. to X. Treatment of X with MeOH-HCl gave I (R = Me).
IT **29169-51-5P 29217-57-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 29169-51-5 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acrylamide, 5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-, benzoate (ester), (E)-(S)-(+)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

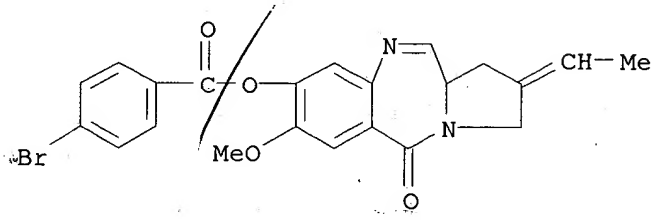


RN 29217-57-0 CAPLUS

L26 ANSWER 105 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1970:477291 CAPLUS
DN 73:77291
TI Microbicidal and antitumorous 2-ethylidene-7-methoxy-8-hydroxy-1,2,3,10,11,11a-hexahydro-5H-pyrrolo [2,1-c] [1,4]benzodiazepin-5-ones from a new Streptomyces
IN Arima, Kei; Tamura, Gakuzo; Sakai, Heiichi; Kosaka, Masanobu; Yazawa, Hisatoyo; Kariyone, Kazuo
PA Fujisawa Pharmaceutical Co., Ltd.
SO Ger. Offen., 39 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

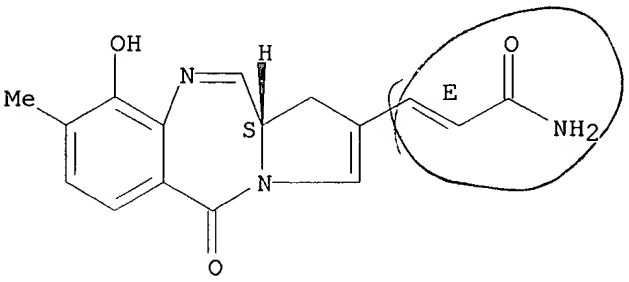
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 1965304	A	19700723	DE 1969-1965304	19691229
	JP 48000076	A2	00000000	JP 1969-83	19681230
	JP 48043755	B4	19731220	JP 1969-50780	19690626
	IL 33558	A1	19731025	IL 1969-33558	19691217
	ZA 6908792	A	19710331	ZA 1969-8792	19691218
	FI 46259	B	19721031	FI 1969-3710	19691222
	GB 1299198	A	19721206	GB 1969-1299198	19691224
	FR 2027356	A5	19700925	FR 1969-45316	19691229
	FR 2027356	B1	19740111		
	SU 474148	D	19750614	SU 1969-1877791	19691229
	CH 531564	A	19730131	CH 1969-531564	19691230
	CH 539062	A	19730831	CH 1972-7606	19691230
	CA 955595	A1	19741001	CA 1970-86357	19700623
	US 3794644	A	19740226	US 1970-49974	19700625
PRAI	JP 1969-83		19681230		
	JP 1969-50780		19690626		
	JP 1968-83		19681230		

GI For diagram(s), see printed CA Issue.
AB The title compds. (I) with antiviral and antibacteriophagic activity were prepd. by microbiol. formation of the powdery fundamental substance by means of the new S. achromogenes var tomaymyceticus ATCC 21353 and subsequent chem. reactions. Thus, the supernatant of a culture medium of ATCC 21353 was extd. to give a powder, which gave with MeOH at -20.degree. I (R = OMe, R1 = H) (Ia). Similarly prepd. was I (R = OEt, R1 = H). Heating Ia in CHCl3 or AcOEt gave II (R1 = H) (IIa), which added MeOH to regenerate Ia. Ia and CH2N2, Ac2O-pyridine, or (p-BrC6H4CO)2O-pyridine gave I (R = OMe, R1 = Me), I (R = OMe, R1 = Ac), or crude I (R = OMe, R1 = p-BrC6H4CO), resp. Treating the latter with MeCN gave II (R1 = p-BrC6H4CO. IIa and PhCH2SH, EtSH, or Me2NH gave I (R = PhCH2S, R1 = H), I (R = EtS, R1 = H), or I (R = Me2N, R1 = H). The uv and ir spectra of Ia and its activity against several microorganisms were reported.
IT **28797-41-3P 28797-43-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 28797-41-3 CAPLUS
RN 28797-43-5 CAPLUS
CN Benzoic acid, 4-bromo-, 2-ethylidene-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl ester (9CI) (CA INDEX NAME)


O
C
O
N
CH—Me
Br
MeO
N
O

L26 ANSWER 106 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1968:85851 CAPLUS
DN 68:85851
TI Spectrophotometric studies of the interaction of anthramycin with deoxyribonucleic acid
AU Stefanovic, Vladimir
CS Hoffmann-LaRoche., Inc., Nutley, N. J., USA
SO Biochem. Pharmacol. (1968), 17(2), 315-23
CODEN: BCPCA6
DT Journal
LA English
AB Qual. and quant. aspects of the interaction between anthramycin Me ether (I) and DNA were investigated spectrophotometrically by utilizing alterations in the I spectrum that result from complex formation. Certain nucleic acid polymers, purine and pyrimidine derivs., and various agents were employed in examg. the mol. nature of the interaction. These expts. suggest that binding involves both electrostatic attraction between I and the anionic phosphate groups of DNA, and a more specific interaction apparently involving 7-membered ring portions of I and DNA. The secondary structure of DNA also affects its binding to I. The ability of the compds. of the anthramycin series to complex with DNA was correlated with their biol. activity. The possibility of predicting biol. activity of a new compd. from this series by using only spectrophotometric assay is therefore indicated.
IT **16758-27-3**
RL: BIOL (Biological study)
(complexing of, with deoxyribonucleic acid, antibiotic activity in relation to)
RN 16758-27-3 CAPLUS
CN 2-Propenamide, 3-[(11aS)-5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



see 101 of 107

L26 ANSWER 107 OF 107 CAPLUS COPYRIGHT 2001 ACS
AN 1968:58569 CAPLUS
DN 68:58569
TI 5-Oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2- acrylamides
IN Berger, Julius; Karr, Andrew E.; Leimgruber, Willy; Schocher, Arno J.; Stefanovic, Vladimir; Tabenkin, Benjamin
PA Hoffmann-la Roche Inc.
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3361742	A	19680102	US 1964-416599	19641207
	FR 1553664	A	19690117	FR 1965-1553664	19651203
	BE 673376	A	19660401	BE 1965-673376	19651207
	NL 6515880	A	19660608	NL 1965-15880	19651207
	CH 475997	A	19690731	CH 1965-475997	19651207
	SE 316136	B	19691020	SE 1965-15830	19651207
	BR 6575537	A0	19730906	BR 1965-175537	19651207
PRAI	US 1964-416599	A	19641207		

GI For diagram(s), see printed CA Issue.

AB The title compds., having antibacterial and anticancer activity are produced by culturing Streptomyces refuineus var thermotolerans, NRRL 3143 or 3144. Extn., purification, and crystn. yields 5,10,11,11a-tetrahydro-9-hydroxy- 11 - methoxy - 8 - methyl - 5 - oxo - 1H - pyrrolo 2,1-c] 1,4]benzodiazepin-2-acrylamide (I). X is 0-1.5. I, when heated with a nonalc. inert solvent (Me2SO, MeCN, Me2CO) at 50.degree.-200.degree. yields II. II, when treated with H2O, yields III. III, when treated with an alc. (Me, Et, Bu, benzyl, .beta.-aminoethyl alc.), a sugar (mannitol), or ethylene glycol, yields IV. Thus, several loopfuls of spores of Streptomyces species NRRL 3143 were transferred from a mature (2-3-day-old) 45.degree. stock agar slant to 100 ml. of medium contg. Bacto tryptone 5, Bacto yeast ext. 2, Bacto soytone 2, sol. starch 10, and mannitol 5 g., MgSO4.H2O 200, Fe(NH4)2(SO4)2.6H2O 10, MnCl2.4H2O 1.8, ZnCl2 2.1, CuSO4 H2O 0.3, Co(NO3)2.6H2O 0.5, and H3BO3 0.6 mg./l. in a 1-l. Blake bottle. The medium was incubated at 45.degree. on a rotary shaker for 16 hrs. The contents of 2 Blake bottles were pooled into a 500-ml. transfer bottle fitted with a tubulature at the bottom and contg. 150 ml. of sterile water. The contents were transferred to a 100-gal. stainless steel fermentor prepd. as follows: to 25 gal. of tap water in the fermentor were added potato starch 1500, enzyme-hydrolyzed casein 750, enzyme-hydrolyzed soy protein 300, aq. ext. of yeast 300, mannitol 750, MgSO4.7H2O 30, Fe(NH4)2(SO4)2.6H2O 1.5, and Dow Corning Silicone A emulsion 2.5 g., MnCl2.4H2O 270, ZnCl2 315, CuSO4.5H2O 45, Co(NO3)2.6H2O 75, H3BO3 90 mg. When all the ingredients were dissolved, the vol. was brought to 40 gal. with tap water and the pH adjusted to 7.2 with 60 ml. of 5N KOH. The medium was sterilized by heating to and holding at 120.degree. for 30-40 min. The batch was cooled and inoculated as above. Aeration with 3 cu. ft. of air/min., agitation at a shaft speed of 400 rpm., and a temp. of 48.degree. were used. Sterile 2.5% suspension of Dow Silicone Emulsion AF for control of foam was added as needed. Hourly samples were taken from the 12th hr. on and assayed for in vitro potency. The batch reached its max. potency in 18-20 hrs. The above process was repeated 10 times. The broths were combined, the pH adjusted to 6, and the broth was filtered. The filtrate was extd. countercurrently at 128 gal./hr. with the same rate of BuOH in a Karr extn. column. A water

backwash of 0.2 times the BuOH rate was used at the top of the column to minimize the carryover of water-sol. components. The BuOH ext. was concd. to .apprx.a 5% soln. which was the feed to a Karr fractional liquid extn. column. The column was operated at a H2O-BuOH ratio of 10:1 and the BuOH ext. contained the product; the ext. was concd. to a soln. or paste contg. 5-20% solids; 25-50 vols. of n-C6H14 was added and the resulting slurry filtered. The pptd. product was vacuum-dried.

IT **14435-72-4P**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manuf. of)

RN 14435-72-4 CAPLUS

CN 2-Propenamide, 3-(5,10,11,11a-tetrahydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)- (9CI) (CA INDEX NAME)

proviso Ia